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EPIDEMIC ENCEPHALITIS *

A FOLLOW-UP STUDY OF TWO HUNDRED AND SIXTY-SIX CASES

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BOSTON

In a total of 303 cases the diagnosis of epidemic encephalitis was made at the Boston Psychopathic Hospital up to the end of 1934. Only 7 patients had the first symptoms prior to 1917; 25 had the acute attack after the end of 1926. The remaining 271 patients had the first symptoms in the epidemic years from 1917 to 1926 and were arbitrarily selected for this report. As a result of this investigation, 5 of the 271 patients were found to have been suffering from conditions other than epidemic encephalitis, namely cerebral syphilis, Sydenham's chorea, alcoholism and tumor of the brain, and were excluded. Of the total of 266 patients, information was obtained concerning the present condition of 240. Seventy-eight of these were admitted to the hospital within the first three months after the onset of symptoms. The remainder, or 162 patients, were afflicted with sequelae or were in a chronic stage when they first came under observation. It is now generally recognized that epidemic encephalitis occurring in the period covered by this study was an infectious, chronic, progressive process. The need for prolonged periods of observation before attempting to evaluate end-results is obvious. The meagerness of such published observations is striking and prompted the present report.

This study was made with the help of two social workers, who made visits to interview 31 patients at their homes. I examined 61 survivors. Ninety-four patients had died. The private physicians of 8 patients made reports. Forty-six patients could not be interviewed (19 had left the state), and in these cases a nontechnical questionnaire answered by the patient or relatives was the only source of information. Observations on the 100 patients interviewed or examined were made more complete and uniform by the use of a technical questionnaire. The social workers were trained in its use with patients with chronic encephalitis at the clinic.

From the Boston Psychopathic Hospital.

* The term epidemic encephalitis is used in this paper to designate encephalitis lethargica, described by von Economo.

The proportion of survivors without evidence of sequelae among the 61 patients examined by me was 1.6 per cent, but I saw a selected group, including all the patients now in hospitals or attending the outpatient clinic. Cooperating physicians reported 1 case of complete recovery among 8 patients under their care. The proportion of patients with complete recovery among the 31 patients interviewed in their homes by the social workers was 22.6 per cent. In the 46 instances in which patients or their relatives answered questionnaires, 19.5 per cent of persons with complete recovery was reported. That the proportion of recoveries in these two groups of patients agrees so well is taken as evidence that patients and their relatives who answered questionnaires gave as complete and reliable information as trained social workers could obtain by interview. It was expected that the great majority of patients who recovered would be seen in their homes by the social workers or would be so widely scattered as to necessitate dependence on correspondence. This was found to be the case.

In 13 instances patients or their relatives claimed that complete recovery had been made, but either symptoms were reported or signs were found which nullified the claim. These patients showed wide variation in the degree of incapacity but were in no case classified as completely recovered. The sometimes striking inconsistency of the condition with the claim to recovery is in some part explained by the euphoria present in some cases as a sequel to the disease. Some late-appearing symptoms are not recognized by patients as due to the preceding infection. Rarely, a patient or relative was found to be antagonistic, and the denials were essentially protests. In the minds of some patients encephalitis is associated with syphilis, and evidence of it, like mental disease, is concealed as something shameful.

The 266 patients studied may be divided into three groups on the basis of the duration of observation, these three categories having an inverse ratio to the duration of the illness before the patient came under observation. Patients in these groups may be designated as having acute, chronic or late stages, respectively. Group 1 (83 persons) consists of patients admitted in the period from 1920 to 1926 within three months after the onset of acute symptoms and observed again after from ten to sixteen years, the mean being fourteen years after the acute attack. Group 2 (106 persons) consists of patients with sequelae or those in the chronic stage admitted in the period from 1919 to 1926, within a few years after the acute attack. These patients have again come under observation from ten to seventeen years later, the mean for the group being twelve years. Group 3 (77 persons) consists of patients later in the course of the disease, having been first admitted in the period from 1927 to 1934. The acute symptoms had occurred in the same period as those of patients in group 2, namely, in the years from 1917 to 1926. Patients in group 3 have again come under observation

from two to nine years later, the mean being six years. Table 1 presents a summary of the present condition of the patients in these three groups. The proportion of patients who are alive and apparently recovered is highest (11.5 per cent) in group 1, i. e., in patients who had had symptoms for the shortest time prior to admission. The proportion of patients without sequelae is lowest (1.4 per cent) in group 3, i. e., in patients who were admitted with manifest symptoms at the longest time after the acute attack of encephalitis. In addition, the patients in group 3 have been followed for a shorter time during which recovery might have occurred. Group 2 showed a ratio of recovery of 7.7 per cent—an intermediate figure, as would be expected.

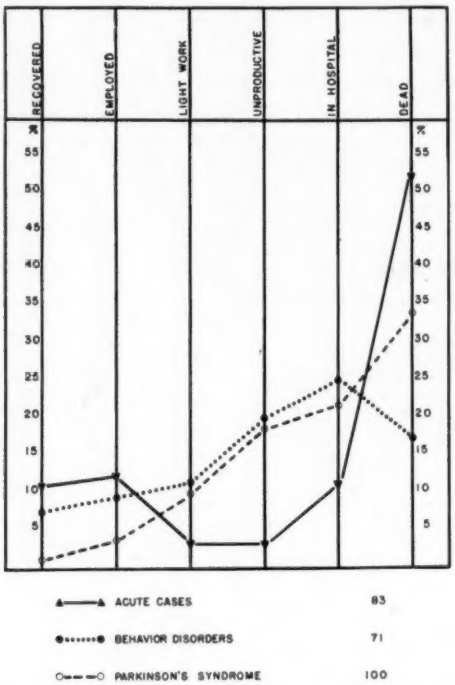
TABLE 1.—*Condition in 1936 of 266 Patients with Epidemic Encephalitis Admitted to the Boston Psychopathic Hospital, Grouped According to the Stage of Illness and Length of Observation*

	Acute Stage, Group 1	Chronic Stage		Total Number
		Group 2	Group 3	
Total number of cases in each group	83	106	77	266
Mean of length of observation, years	14	12	6	10.8
Patients not found	5	16	5	26
Total number of patients found or whose status was determined	78	90	72	240
Recovered patients seen	3	4	1	8
Recovered patients not seen	6	3	0	9
Total number of living patients seen	19	36	45	100
Living patients not seen, status known	16	17	13	46
Patients mistakenly claiming recovery	6	5	2	13
Patients now employed, not recovered	10	8	4	22
Patients able to do light work, not recovered	3	7	14	24
Patients entirely unproductive, outside hospital	3	15	16	34
Patients now in hospitals for chronic invalids	1	3	3	7
Patients now in hospitals for mental disease	8	14	20	42
Patients admitted to other hospitals for mental disease	25	65	46	136
Patients who died in hospitals for mental disease	34	18	11	63
Deaths from all causes	44	36	14	94
Median age at time of acute attack	30	16	12	19
Median age at admission	30	20	20	23
Median age of survivors	40	30	27	31
Median age at death	35	27	23	32
Median of years from onset to death	—1	10	10	7
Males in each group	53	55	52	160
Median age of recovered patients at time of admission	33	18	15	24
Median age of recovered patients at acute attack	33	18	6	23

Table 1 also presents statistical facts regarding the age of patients in the three groups at the time of the acute attack and on admission. The difference in the ages of patients in group 1 and of those in groups 2 and 3 is striking. The long duration of the illness once it enters the chronic phase is evident in that the 50 patients in groups 2 and 3 who died had lived for an average of ten years. The predominance of males is in keeping with a similar predominance among all patients admitted to the Boston Psychopathic Hospital.

The 266 patients may be further classified as to the chief disorder present when they were first admitted to the hospital. Table 2 summarizes the present condition of the patients in the various clinical groups. Three large groups—those in the acute stage, those with behavior disorders and those with Parkinson's syndrome—together include

over 95 per cent of all patients. The end-results for these three groups are presented graphically in the chart. Every classification does violence to individual symptomatology, which here too shows a marked tendency to an overlapping clinical picture. When a behavior disorder and Parkinson's syndrome were both present, the patient was classified with those showing behavior disorders as a primary grouping. The 100 patients showing chiefly Parkinson's syndrome formed the largest group and had the poorest prognosis for complete recovery. In the single case of this type in which there was complete recovery, tremor and rigidity



Condition in 1936 of 254 patients classified according to the predominant symptoms on admission.

appeared during the acute stage and gradually disappeared during the course of the first few ensuing years. The greatest number of deaths and the largest proportion of persons with complete recovery were found among the 83 patients admitted in the acute stage. Patients with behavior disorders had the fewest deaths, but they were the most incapacitated from a social point of view. Their number, however, accounted for 5 of the 17 patients who recovered.

Other published reports on prognosis give widely varying figures. These are summarized for purposes of comparison in tables 3 and 4 for

groups of patients with the acute and the chronic stage, respectively. The findings of Robb, in Belfast, and of Dennig and his associates, in Germany, were in closest agreement with my figures for recovery of persons in the acute stage. The average for these three observations is 10.9 per cent. Other workers in Europe and the United States have reported figures varying from 0 to 54.5 per cent, the higher figures usually indicating a striking predominance of children. The criteria for diagnosis, as well as for recovery, vary widely, making comparisons

TABLE 2.—*Condition in 1936 of 266 Patients with Epidemic Encephalitis Classified as to Clinical Type at Time of Admission to the Boston Psychopathic Hospital*

Predominant Clinical Picture	Lost	Died	Died in Hospital for Mental Disease	Now in Hospital for Mental Disease	Now in Hospital for Chronic Diseases	Entirely Unproductive	Able to Do Light Work	Employed, Not Recovered	Completely Recovered	Total Number
Acute encephalitis (mean age on admission, 30 yr.)	..	..	..	..	..	..	..	..	..	83
(*a*) Delusions and hallucinations	1	29	24	5	1	2	3	7	5	54
(*b*) Excitement and confusion	2	11	8	3	..	..	..	3	3	22
(*c*) Depression and lethargy	2	4	2	..	..	..	..	..	1	7
Behavior disorders (mean age on admission, 14 yr.)	..	..	..	..	..	..	..	..	..	71
(*a*) Overactivity	2	3	2	11	1	6	6	3	4	36
(*b*) Parkinson's syndrome	2	2	2	4	1	3	1	1	..	14
(*c*) Compulsions and tics	1	5	4	1	..	2	..	1	..	10
(*d*) Somnolence	2	2	..	..	..	1	..	1	1	7
(*e*) Delusions and hallucinations	..	..	..	..	..	2	1	1	..	4
Parkinson syndrome (mean age on admission, 24 yr.)	..	..	..	..	..	..	..	..	..	100
(*a*) Depression	4	10	5	3	3	2	2	2	..	26
(*b*) Delusions and hallucinations	1	9	8	10	..	1	2	..	1	24
(*c*) Somnolence and lethargy	2	10	2	..	..	6	3	..	..	21
(*d*) Irritability and emotionalism	3	2	1	4	1	3	2	1	..	16
(*e*) Oculogyric crises	1	4	2	..	..	4	1	..	..	10
(*f*) Other types	1	1	1	..	..	..	1	..	..	3
Other sequelae (mean age on admission, 23 yr.)	..	..	..	..	..	..	..	..	..	12
(*a*) Delusions and hallucinations	..	..	..	..	..	..	1	2	1	4
(*b*) Depression and somnolence	2	..	..	1	..	..	..	..	1	4
(*c*) Mental deterioration and epilepsy	..	2	2	..	..	1	1	..	..	4
Total number of cases	26	94	63	42	7	34	24	22	17	266

difficult and often misleading. The prognosis for complete recovery is very poor for adults with sequelae, according to all observers, but is distinctly better for children. This disparity is due to the great frequency of behavior disorders among children who have had encephalitis, whereas that syndrome is all but unknown if maturity has been reached before onset of the disease. Reports of patients with Parkinson's syndrome who recover are extremely rare. The proportion of persons with complete recovery among the 162 patients with sequelae in the present study was 4.9 per cent, the majority occurring in the group of patients with behavior disorders.

The chief causes of death in the 94 cases of fatality were as follows: Epidemic encephalitis was the cause of death in 49 instances, in half of which death occurred within the first year after onset of symptoms. Pulmonary tuberculosis was responsible for 15 deaths. Bronchopneumonia and suicide each accounted for 5 deaths. Other less frequent causes of death were atrophy of the adrenals, diabetes mellitus, nephritis, cerebral hemorrhage, chronic myocarditis, perforated peptic ulcer,

TABLE 3.—*Prognosis for Complete Recovery After an Acute Attack of Epidemic Encephalitis*

Author	Year	No. of Patients Found	Duration of Observation, Years	Deaths in Acute Stage, %	Deaths in Chronic Stage, % of Patients Found	Patients Lost, %	Complete Recovery, % of Patients Found
Cruchet, R.: Bull et mém. Soc. méd. d. hôp. de Paris **45**: 344 (March 11) 1921	1921	32	...	37.5	....	....	0
Bing, R., and Staehalin, R.: Schweiz. med. Wchnschr. **52**: 142-144 (Feb. 9) 1922	1922	97	...	17.0	....	....	25.0
Grossman, M.:* Sequels of Acute Epidemic Encephalitis: A Study of Ninety-Two Cases from One to Three Years After Recovery, J. A. M. A. **78**: 959-962 (April 1) 1922....	1922	92	2	....	....	....	10.8
Anderson, G. H.:† Quart. J. Med. **16**: 173-192 (April) 1923	1923	40	3	17.5	....	....	0
Dennig, H., and von Philipsborn, E.: Deutsche med. Wchnschr. **49**: 1418-1419 (Nov. 9) 1923	1923	68	3	26.0	....	5.6	12.5
Neal, J. B., and others:‡ Am. J. M. Sc. **170**: 708-722 (Oct.) 1925	1925	415	4	28.2	....	10.0	54.5
Robb, A. G.: Brit. M. J. **1**: 615-616 (April 2) 1927	1927	162	2.5	12.1	4.9	6.4	8.8
Ziegler, L. H.: Follow-Up Studies on Persons Who Have Had Epidemic Encephalitis J. A. M. A. **91**: 138-141 (July 21) 1928	1928	41	5.5	31.7	....	21.6	17.0
Howe, H. A.:† Bull. Johns Hopkins Hosp. **47**: 123-156 (Sept.) 1930	1930	66	8	12.0	4.5	42.6	42.0
Strömbäck, G.: Acta med. Scandinav., 1932, supp. 50, pp. 150-166....	1932	102	9	8.4	8.4	5.0	18.6
Sauter, E.:* Schweiz. med Wchnschr. **64**: 464-469 (May 19) 1934	1934	34	12	....	17.6	15.0	46.0
Boston Psychopathic Hospital, group 1	1936	78	14	32.0	24.4	6.4	11.5

* Only survivors from the acute stage were studied.
† Only children were studied.
‡ Children predominated.

carcinoma of the cervix, erysipelas, septicemia and accidental insufflation of food; in 3 cases the cause of death was unknown. Epidemic encephalitis was a contributing factor in over one half of the deaths not directly attributed to it.

The degree of incapacity varied widely in patients showing sequelae. A dozen were bed fast; at the other extreme were 22 patients who were employed and self-supporting, some of whom were accepted by the community as normal. Of the 129 patients with sequelae still living,

obvious Parkinson's syndrome was present in 51.5 per cent. Table 5 lists the disturbances now present in order of their frequency.

Of the 240 patients followed successfully 56.9 per cent were admitted to other hospitals for mental disease, and 28.5 per cent of the 146 survivors were in a hospital for mental disease in 1936. This is doubtless not representative of the incidence of hospitalization for mental symptoms in an unselected group of patients with epidemic encephalitis in Massachusetts. As Boston is served by both general hospitals and hospitals for mental diseases, patients with prominent mental disturbances

TABLE 4.—*Prognosis for Complete Recovery of Patients with Epidemic Encephalitis Showing Chronic Sequelae*

Author	Year	No. of Patients Found	Duration of Observation, Years	Onset to Final Observation, Years	Deaths in Chronic Stage, % of Patients Found	Patients Lost, %	Complete Recovery, % of Patients Found
Kennedy, R.:* The Prognosis of Sequelae of Epidemic Encephalitis in Children, Am. J. Dis. Child. **28**: 158-172 (Aug.) 1924	1924	51	3	3	2.0	13.5	22.0
Dennig, H., and Voellm, R.: Deutsches Arch. f. klin. Med. **155**: 257-262 (June) 1927	1927	129	3	6	10.8	6.5	8.0
Sprunt, T. P.: Am. J. M. Sc. **174**: 660-665 (Nov.) 1927	1927	35	5	..	3.0	30.0	14.3
Ziegler, L. H.:‡ Follow-Up Studies on Persons Who Have Had Epidemic Encephalitis, J. A. M. A. **91**: 138-141 (July 21) 1928	1928	711	..	5.5	11.9	56.3	0.4
Eyrich, M., and Eyrich, H.:* Ztschr. f. d. ges. Neurol. u. Psychiat. **117**: 620-648, 1928	1928	68	8	8	2.9	4.2	2.9
Renaud, M., and others:† Bull. et mém. Soc. méd. d. hôp. de Paris **48**: 1661-1665 (Dec. 16) 1932	1932	44	10	10	59.1	32.3	0
Hall, A. J.:† Lancet **2**: 147-148 (July 20) 1935	1935	289	..	12	26.6	42.2	0
Boston Psychopathic Hospital							
Group 2	1936	90	12	14	40.0	15.1	7.7
Group 3	1936	72	6	14	19.4	6.4	1.4
Total number, groups 2 and 3		162	9.5	14	30.9	11.4	4.9

* Only children were studied.
† Only patients with Parkinson's syndrome were studied.
‡ Patients with Parkinson's syndrome predominated.

are less likely to be accepted by general hospitals. Even so, I found that 6.4 per cent of 500 patients with epidemic encephalitis admitted to four large general hospitals in Boston were later admitted to hospitals for mental disease in the state. A total of nearly 600 patients with epidemic encephalitis have been admitted to the hospitals under the jurisdiction of the Massachusetts State Department of Mental Diseases. This is 6 per cent of the estimated total of 10,000 patients with epidemic encephalitis in Massachusetts in the period from 1917 to 1934. This estimate of the total number of these patients is based on the fact that of 1,576 cases of epidemic encephalitis compiled by me from nineteen widely scattered Massachusetts hospitals, only 11.9 per cent were

reported to the State Department of Health, and a total of only 1,150 cases were reported for the entire state. It appears reasonable to believe, therefore, that eight or nine times as many cases occurred as were reported (epidemic encephalitis was made notifiable in Massachusetts in March 1921).

The frequency of further hospitalization for mental disorders among patients admitted to the Boston Psychopathic Hospital with epidemic encephalitis is so high (56.9 per cent) as to make it obvious that these patients are not in all respects similar to those admitted to general hospitals. Is this dissimilarity manifest in the frequency of physical signs and significant laboratory findings? The findings for patients with epidemic encephalitis in the general hospitals in Boston are not known to

TABLE 5.—*Disturbances Found in 1936 in 129 Patients with Sequelae of Epidemic Encephalitis, Tabulated According to Frequency*

Tremor	79	Strabismus	12
Emotional disturbance	71	Pains and paresthesias	12
Parkinson's syndrome	67	Increase in appetite	11
Disturbance in speech	60	Headache	11
Rigidity	56	Adiposity	10
Sleepiness	41	Diplopia	9
Depression	36	Loss of weight	8
Loss of intelligence	36	Nystagmus	7
Change in personality	33	Phobias and compulsions	7
Increased activity	26	Difficulties in swallowing	5
Euphoria	25	Pituitary dysfunction	4
Oculogyric crises	21	Mental deficiency	4
Paresis of a limb	20	Narcolepsy	4
Loss of memory	19	Schizophrenic syndrome	4
Vegetative disturbances	18	Manic-depressive syndrome	4
Decreased activity	18	Chorea	3
Delusions	18	Tinnitus	3
Disorders of conduct	16	Deafness	3
Hallucinations	15	Loss of appetite	2
Convulsions	14	Anxiety state	2
Insomnia	13	Blindness	1
Ptosis	12	Catalepsy	1

me, but I presume their incidence is similar to figures reported elsewhere. In table 6 the commoner physical signs and symptoms are tabulated in order of their frequency among the 266 patients at the time of first coming under observation. The same physical syndromes are found here as in patients at the general hospitals. The observations on the spinal fluid and other common laboratory findings are also comparable. The two groups differ essentially in the prominence of mental symptoms, which make the patient with encephalitis a difficult problem in a general hospital. The mental symptoms and disorders of conduct present on admission are given in table 7.

The sequelae of epidemic encephalitis have an economic and a social significance. Two patients committed impulsive murders. A number have appeared repeatedly in the courts. Three are in disciplinary schools, and 1 is serving a long sentence in a reformatory. Of the 129 survivors who have not recovered only 22 are self-supporting, and 49 are receiving

semipermanent institutional care, chiefly at public expense. The only patients that may be expected to show further improvement in the present series are the younger patients with behavior problems. Of the 48 survivors falling into this group who did not recover, 10 have Parkinson's syndrome, with a bad prognosis for recovery. If one excludes

TABLE 6.—*Frequency of Commonest Signs and Symptoms in 266 Patients with Epidemic Encephalitis at the Time of First Admission to the Boston Psychopathic Hospital*

Ocular disturbances, all types	247	Dysarthria	53
Disturbances in sleep, all types	240	Weakness of an extremity	52
Both ocular and sleep disturbances	201	Cardiac disturbances	50
Somnolence	186	Incontinence	46
Tremor	186	Vomiting	45
Insomnia	137	Chorea	42
Masklike facies	134	Stooping	42
Sluggishness of pupils to light	115	Monotonous speech	42
Headache	113	Blurred vision	40
Slowness of movement	109	Loss of arm swing with walking	40
Delirium	103	Myoclonia	36
Diplopia	97	Drooling	36
General rigidity	96	Paresthesias	35
Fever	96	Sweating	35
Neuritic pains	83	Convulsions	34
Asthenia	81	Increased sex drive	32
Irregularity of pupils	78	Ties	31
Ptosis	73	Increase in appetite	30
Twitching	72	Cyanosis	27
Unequality of pupils	69	Obesity	24
Stupor	69	Oculogyric crises	21
Festinant gait	67	Respiratory disturbances	20
Weakness of the face	61	Marked loss of weight	20
Strabismus	61	Fainting attacks	19
Sluggishness of pupils in accommodation	59	Dysphagia	18
Dizziness	59	Marked flushing	16
Nystagmus	58	Blindness	16
Inversion of sleep rhythm	56	Increased salivation	15

TABLE 7.—*Frequency of Mental Symptoms and Behavior Disorders Present on Admission in 266 Patients with Epidemic Encephalitis at the Boston Psychopathic Hospital*

Depression	149	Disobedience	49
Increased activity	103	Fear	48
Irritability	97	Increased talkativeness	47
Hallucinations	97	Lowered intelligence	42
Delusions	93	Acute excitement	25
Euphoria	83	Stealing	25
Retardation of thought	83	Running away	25
Prolonged excitement	82	Cruelty	23
Emotional instability	82	Sexual perversions	18
Defect in memory	79	Compulsive acts	12
Apathy	62	Sexual assaults	7
Delusions and hallucinations with delirium	60	Obsessive thoughts	3

these 10 patients with progressing physical handicaps, there are 38 patients, a considerable number of whom may yet be salvaged. Of the 43 patients previously showing behavior disorders and no definite physical incapacity, 5 have completely recovered and 6 others are employed and self-supporting, or a total of 25.6 per cent of these patients are recovered or employed. This figure compares favorably with the 24 per cent of

patients with "postencephalitic behavior disorders" who are doing well in their homes after a period in a special hospital training school, as reported by Bond and Smith.[1] Special training schools for patients with postencephalitic behavior problems are of distinct value to the community, though with the passage of time children improve with even the ordinary present facilities. The training school under medical supervision is free from much of the social stigma attached to the disciplinary schools for the juvenile delinquent and is more successful with the postencephalitic child, with whom the usual disciplinary measures fail. Medical supervision of the postencephalitic child in an institution protects both the child and the community. Recidivism is prevented, and the homes of these unfortunate children are vastly improved when the patients are adequately cared for.

CONCLUSIONS

1. Of 78 patients first seen in the acute stage at the Boston Psychopathic Hospital whose condition was diagnosed as epidemic encephalitis, 11.5 per cent are alive and without known sequelae after from ten to sixteen years. The prognosis for lasting recovery appears not to be altered appreciably by the prominence of mental symptoms during the acute attack, for other authors have recorded similar rates of recovery for patients in general hospitals.

2. Of 90 patients with sequelae observed again after from ten to seventeen years, 7.7 per cent are apparently recovered. For 72 patients with sequelae who came under observation more recently, but after a longer elapsed time since the acute attack, the rate of recovery is 1.4 per cent. Children with behavior disorders constitute the only group with sequelae of epidemic encephalitis in whom improvement may reasonably be expected.

79 Phillips Street.

1. Bond, Earl D., and Smith, Lauren H.: Post-Encephalitic Behavior Disorders: A Ten Year Review of the Franklin School, Am. J. Psychiat. **92**:16-33 (July) 1935.

DEGENERATION OF THE *BOUTONS TERMINAUX* IN THE SPINAL CORD

AN EXPERIMENTAL STUDY

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The *boutons terminaux* are generally believed to be the end-processes of axons synapsing on the body and dendrites of a nerve cell (Liddell [1]). In the spinal cord they are known to undergo rapid degeneration when the axon is cut. On this phenomenon depends the *bouton* method for describing the terminal arborization of fiber pathways. While the Marchi and Weigert methods may be successfully used to trace fiber tracts, they leave, nevertheless, the minute nonmyelinated nerve endings unstained. The *bouton* technic offers the best means of studying interrupted fiber pathways at their ultimate termination, and it has therefore a very wide field of application. The increasing use of the method has demanded a set of standards by which to judge stages of degeneration. The attempt is made here to correlate the relevant data on *bouton* degeneration scattered through the literature and to present pictorially the observations based on a study at regular intervals of some stages of degenerating *boutons terminaux* in the cat after section of the spinal cord.

REVIEW OF LITERATURE

The first published description of the termination of adult axons was that of Cajal [2] in 1888. His statement that the collaterals in the spinal cord end *sur la cellule au moyen d'une varicosité en contact avec la membrane* (on the cell through a varicosity in contact with the cell membrane) was confirmed by Kölliker [3] in 1890, and later by Van Gehuchten, von Lenhossek and Retzius [4] in 1893. In 1891 Cajal stated that the pyramidal cells terminated *par un bout rond et un peu épaissi* (in a round and somewhat thickened end).

From the Montreal Neurological Institute.

1. Liddell, E. G. T.: Spinal Shock and Some Features in Isolation-Alteration of the Spinal Cord in Cats, Brain **57**:386-400, 1934.

2. Ramón y Cajal, S.: Les preuves objectives de l'unité anatomique des cellules nerveuses, Trav. du lab. de recherches biol. de l'Univ. de Madrid **29**:1-137, 1934. All citations from Ramón y Cajal are found in this paper.

3. Kölliker, cited by Ramón y Cajal.[2]

4. Retzius, cited by Ramón y Cajal.[2]

Held,[5] in 1897, discovered the protoplasmic endings of axons, which have since been known as the *Endfüsse*. This work was confirmed by Auerbach [6] in 1899, who gave the structures the name *boutons terminaux*. It was not until 1903 that Cajal brought histologic proof of the fibrillar connection between the axon and the *bouton*. Joris,[7] Van Gehuchten [8] and Marinesco confirmed the earlier work on these interneuronal junctions and cited them as proof of "contact" rather than of "continuity" in the synapse.

Cajal compared the *boutons* to the spots on a tiger's skin, and Marinesco likened them to spermatozoa. Golgi [9] suggested that their function is nutritional.

Boutons terminaux have been reported by many authors—in the spinal cord and cerebellum by Hoff [10] and Windle and Clark;[11] in the cerebrum by Cajal, Hoff and Lorente de Nó,[12] and in the sympathetic ganglia by Lawrentjew [13] and de Castro.[14]

Hoff was unable to detect *boutons* in the cords of cats less than 21 days old, and it is thought that their appearance is "sporadic" within the month following birth. (Cajal [2]). Lache [15] drew attention to the fact that there are various sizes of *boutons*, both on the cell bodies and on the dendrites.

Studies of the phenomena of *bouton* degeneration have been made on both experimental and clinical material. In cases of Friedreich's

5. Held, H.: Beiträge zur Struktur der Nervenzellen und ihrer Fortsätze, Arch. f. Anat. u. Entwcklngsgesch., 1897, pp. 204-294.

6. Auerbach, L.: Das terminale Nervennetz in seinen Beziehungen zu den Ganglienzellen der Centralorgane, Monatschr. f. Psychiat. u. Neurol. **6**:192, 1899.

7. Joris, H.: Nouvelles recherches sur les rapports anatomiques des neurones, Mém. couron. Acad. roy. de méd. de Belgique **18**:1-126, 1903.

8. Van Gehuchten, A.: Boutons terminaux et réseau péricellulaire, Névraxe **6**:217-234, 1904.

9. Golgi, C.: La doctrine du neurone: Théorie et faits, Nord. med. Ark. **7**:1-26, 1907.

10. Hoff, E. C.: Degeneration of the Boutons Terminaux in the Spinal Cord, J. Physiol. **74**:4-5P, 1932.

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12. Lorente de Nó, R.: Studies on the Structure of the Cerebral Cortex, J. f. Psychol. u. Neurol. **45**:381-438, 1934; **46**:113-177, 1934.

13. Lawrentjew, B. J.: Ueber die Erscheinungen der Degeneration und Regeneration im sympathischen Nervensystem, Ztschr. f. mikr.-anat. Forsch. **2**:201-223, 1925.

14. de Castro, F.: Sympathetic Ganglia: Normal and Pathological, in Penfield, W.: Cytology and Cellular Pathology of the Nervous System, New York, Paul B. Hoeber, Inc., 1932, vol. 1, p. 317.

15. Lache, I. G.: Sur les boutons terminaux de la cellule nerveuse, Compt. rend. Soc. de biol. **60**:381-382, 1906.

disease, Estable,[16] in 1931, showed detachment of the *boutons* from cells with which they were once in contact. Changes in structure have been reported by Cajal, by Achúcarro [17] in rabies and by Marinesco [18] in numerous diseases, such as anemia and myelitis. Cajal described changes during periods of hibernation. Mott [19] showed a biochemical change taking place in the peripheral part of a nerve process six hours after it had been severed from the cell body. These observations are of interest here in so far as they throw light on *bouton* degeneration arising from experimental section of fiber paths.

Nikolajew [20] was among the first to use the *bouton* method. After cutting the vagus nerve in the frog he traced the degenerating pericellular endings on the ganglion cells of the heart. With the work of Smirnow [21] as a standard for these synapses, he was able to discover which endings were normal and which were degenerating. This work was confirmed by Lawrentjew, who also used the *bouton* method to determine the exact ending of preganglionic fibers in the superior cervical sympathetic ganglion. Bauer [22] cited the work of Levi and his collaborators, who studied degeneration in nerve processes separated from their cell body in tissue culture. Twelve hours following section the distal segment resembled a "string of pearls," the swellings of which were in the process of fragmentary degeneration.

Hoff [23] published the results of *bouton* degeneration following section of the posterior roots and longitudinal transverse section of the spinal cord in cats. He described swelling and granulation in the early stages, with the appearance of a "moniliform varicosity" on a filament in the center of the *bouton*. The structures were markedly degenerated and opaque after three days, reaching a maximum in four

16. Estable, cited by Ramón y Cajal.[2]

17. Achúcarro, N.: Zur Kenntnis der pathologischen Histologie des Zentralnervensystems bei Tollwut, in Nissl, F., and Alzheimer, A.: Histologie und Histopathologie. Arbeiten über die Grosshirnrinde mit besonderer Berücksichtigung der pathologischen Anatomie der Geisteskrankheiten, Jena, Gustav Fischer, 1909, vol. 3, pp. 142-194.

18. Marinesco, G.: Recherches sur la structure de la partie fibrillaire des cellules nerveuses à l'état normal et pathologique, Rev. neurol. **12**:405-428, 1904.

19. Mott, F. W.: Discussion on the Biophysics and Biochemistry of the Neurone, Brit. M. J. **2**:780-784, 1912.

20. Nikolajew, W.: Zur Frage über die Innervation des Froschherzens, Arch. f. Physiol., supp., 1893, pp. 67-73.

21. Smirnow, A.: Die Struktur der Nervenzellen im Sympathicus der Amphibien, Arch. f. mikr. Anat. **35**:407-424, 1890.

22. Bauer, Karl: Beobachtungen über das Wachstum von Nervengewebe, in vitro, Ztschr. f. mikr.-anat. Forsch. **28**:47-80, 1932.

23. Hoff, E. C.: Central Nerve Terminals in the Mammalian Spinal Cord and Their Examination by Experimental Degeneration, Proc. Roy. Soc., London, s.B **111**:175-188, 1932.

and complete disappearance in six days. His studies have been extended to frogs and rabbits and, more recently, to the spinal cord of monkeys,[24] with substantially the same results. Foerster, Gagel and Sheehan[25] confirmed Hoff's work on the spinal cord of monkeys. They observed *boutons,* normally measuring about 2 by 4 microns, which after hypertrophic degeneration measured 4 by 7 microns. Sereni and Young[26] carried out degeneration experiments on cephalopods, with great success. They showed that section of axons produces degenerative changes in the *bouton*-like extremities in fifteen hours. The process varies inversely with the temperature of the surrounding water and attains a maximum in twenty-four hours, with gradual disappearance of the fragments up to seven days.

Lawrentjew found that from six to eight days is the optimum time for degeneration experiments in the sympathetic ganglia. Kolossow[27] described degeneration of the endings on cells of Auerbach's plexus in various animals seventy-one hours after section of the vagus nerve. In a similar way, the *bouton* method has been successfully applied to synaptic degeneration in the semilunar and the inferior mesenteric ganglion and the ganglia of the digestive and genito-urinary tracts and of the adrenal plexus.

It has been necessary to prove that changes of experimental origin are different from postmortem destruction of the *boutons.* Hoff and Hoff[28] showed that aseptic removal of a portion of the spinal cord of a cat, followed by incubation at 37 C. for twenty-four hours in sterile saline solution, produces granular destruction without swelling of the *boutons.* This condition can be distinguished from the hypertrophy and increased affinity for silver seen in *bouton* degeneration following an operative lesion.

No series of photomicrographs has been published which completely correlates the known facts of *bouton* degeneration, although many isolated illustrations have been found.

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24. Hoff, E. C.: Corticospinal Fibers Arising in the Premotor Area of the Monkey: Distribution of Bouton Terminations, Arch. Neurol. & Psychiat. **33:** 687-697 (April) 1935.

25. Foerster, O.; Gagel, O., and Sheehan, D.: Veränderungen an den Endösen im Rückenmark des Affen nach Hinterwurzeldurchschneidung, Ztschr. f. Anat. u. Entwcklngsgesch. **101:**553-565, 1933.

26. Sereni, E., and Young, J. Z.: Nervous Degeneration and Regeneration in Cephalopods, Pubbl. d. stazione zool. di Napoli **12:**173-208, 1932.

27. Kolossow, N. G.: Observations concernant l'innervation de la voie digestive chez les ruminants, Trav. du lab. de recherches biol. de l'Univ. de Madrid **28:** 345-368, 1932-1933.

28. Hoff, E. C., and Hoff, H. E.: Spinal Terminations of the Projection Fibres from the Motor Cortex of Primates, Brain **57:**454-474, 1934.

In summary, the literature indicates that *boutons terminaux* are structural entities in the nerve synapse (fig. 1) and that their degenerative manifestations provide an accurate method for establishing the termination of axons in fiber tracts.

MATERIAL AND METHODS

A series of five cats was used in this investigation. Females weighing approximately 2 Kg. each were selected, in order that the urine might be easily expressed during the postoperative period. Two of the subjects were given ether as an anesthetic, while the other three received intraperitoneal injections of 0.5 cc. of

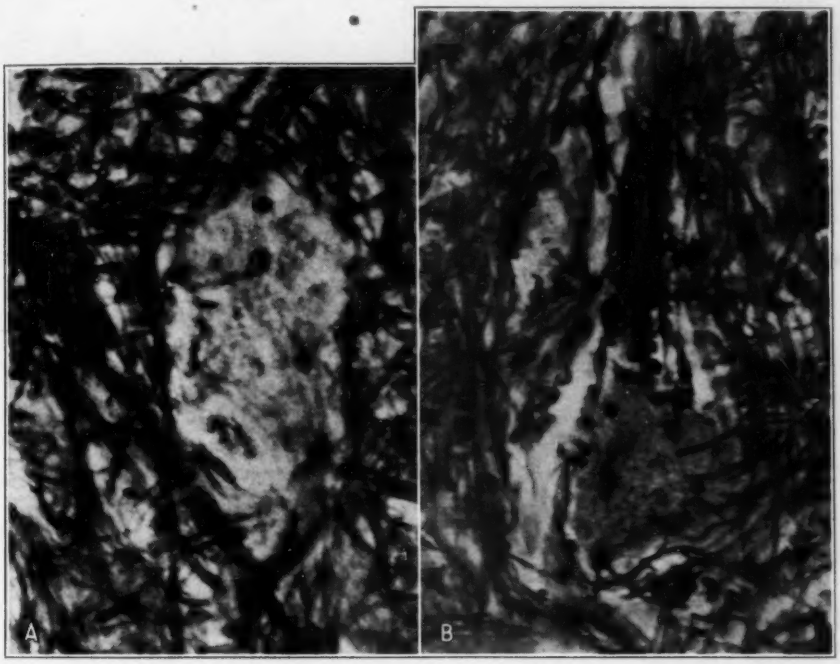

Fig. 1.—Normal *boutons terminaux* on anterior horn cells of the spinal cord in the cat. In *A* is seen a thin fibril ending in a looplike *bouton,* and in *B,* arrangement of the *boutons* on the cell body and dendrites. Magnification, 2,900 diameters.

dial per kilogram of body weight. With aseptic technic, laminectomy was performed at the level of the first lumbar vertebra, the dura being exposed and the bleeding in the bone stopped with bone wax. A similar exposure was made between the eighth and the tenth thoracic vertebra. In the lower exposure the dura was excised lateral to the dorsal spinal artery and reflected from 1 to 2 cm. An aneurysm needle carrying silk thread was passed around the cord intradurally. With slight tension on the thread the cord was completely sectioned with a pair of fine scissors. The same procedure was carried out on the cord at the thoracic level already prepared. Bleeding was thus minimized and a comparatively dry field was the result.

The postoperative course of the animals was uneventful. All were given milk on the first day, the cats which had been anesthetized with ether being more alert. In each case there were paralysis of the hind-quarters and retention of urine.

Killing the cats was essentially the same in all cases. Each animal was placed under ether anesthesia, and a longitudinal incision was made in the abdominal wall. A small cannula was inserted into the abdominal aorta, just above its bifurcation. All branches of the aorta running to abdominal viscera were clamped, special care being taken to "shell out" the kidneys to insure complete obstruction of the renal vessels with forceps. After the brachial arteries had been clamped, 250 cc. of Ringer's solution was slowly injected through the cannula placed in the abdominal aorta. When the injection was well under way, the inferior vena cava was incised, with the result that after a time clear fluid issued from it. Injection of 300 cc. of a 10 per cent solution of chloral hydrate followed that of Ringer's solution without delay, and gradual development of rigor could be seen as the injection progressed.

The spinal cord and brain were quickly removed and placed in a large excess of a 10 per cent solution of chloral hydrate for twenty-four hours. Complete fixation occurred only when the cord had been cut into small blocks, not more than the length of one segment. The staining technic used was Cajal's 6-a reduced silver method, as described by Lee.[29] The blocks were kept in 95 per cent alcohol with seven drops of ammonia per hundred cubic centimeters of alcohol for twenty-four hours. They were then blotted dry, wrapped individually in small pieces of filter paper and immersed in a 2 per cent solution of silver nitrate for seven days, at 37 C. Good results were obtained by adding a small quantity of 95 per cent alcohol to the silver bath and renewing the silver solution after four days. Fifty cubic centimeters of a 2 per cent solution of silver nitrate was found to be sufficient for three small blocks of spinal cord tissue.

After the silver immersion the pieces were unwrapped and thoroughly washed in distilled water. A 2 per cent aqueous solution of hydroquinone or pyrogallol was used for a period of from twenty-four to forty-eight hours to reduce the specimens. The blocks were washed, dehydrated and embedded in paraffin. Serial sections at 15 microns were found to be the best for microscopic analysis of *bouton* degeneration.

RESULTS

Microscopic examination of the *boutons* on ventral and dorsal horn cells in the serial sections revealed a sequence of degenerative modifications analogous to that described by Cajal for the peripheral stumps of sectioned nerve processes. *Boutons* which had been separated from their cell body for twenty-four hours showed a uniform swelling (fig. 2). Their diameter increased from 2 to 2.4 microns on the average, and the looplike appearance was gradually lost. This stage is an early form of what Cajal described aptly as "premonitory of fragmentation."

After forty-eight hours the degenerating *bouton* had lost its central hollow and its circular configuration (fig. 3). It was characterized by

29. Lee, Arthur Bolles: The Microtomist's Vade-Mecum: A Handbook of the Methods of Microscopic Anatomy, ed. 9, Philadelphia, P. Blakiston's Son & Co., 1928.

Fig. 2.—Terminal *boutons* twenty-four hours after section of their axis-cylinders. Their ringlike appearance is preserved, though they are considerably swollen. The normal *bouton* on the center of the anterior horn cell is easily differentiated. Magnification: 2,900 diameters.

Fig. 3.—Degenerated terminals forty-eight hours after section of the spinal cord. Note the large anterior horn cell with opaque *boutons* in contact with the periphery. Magnification: 2,900 diameters.

irregular varicosities, which increased its breadth from 2.4 to 2.8 microns. In common with the adjacent neurofibrillar tissue, the degenerating *bouton* showed an increased affinity for the silver salts.

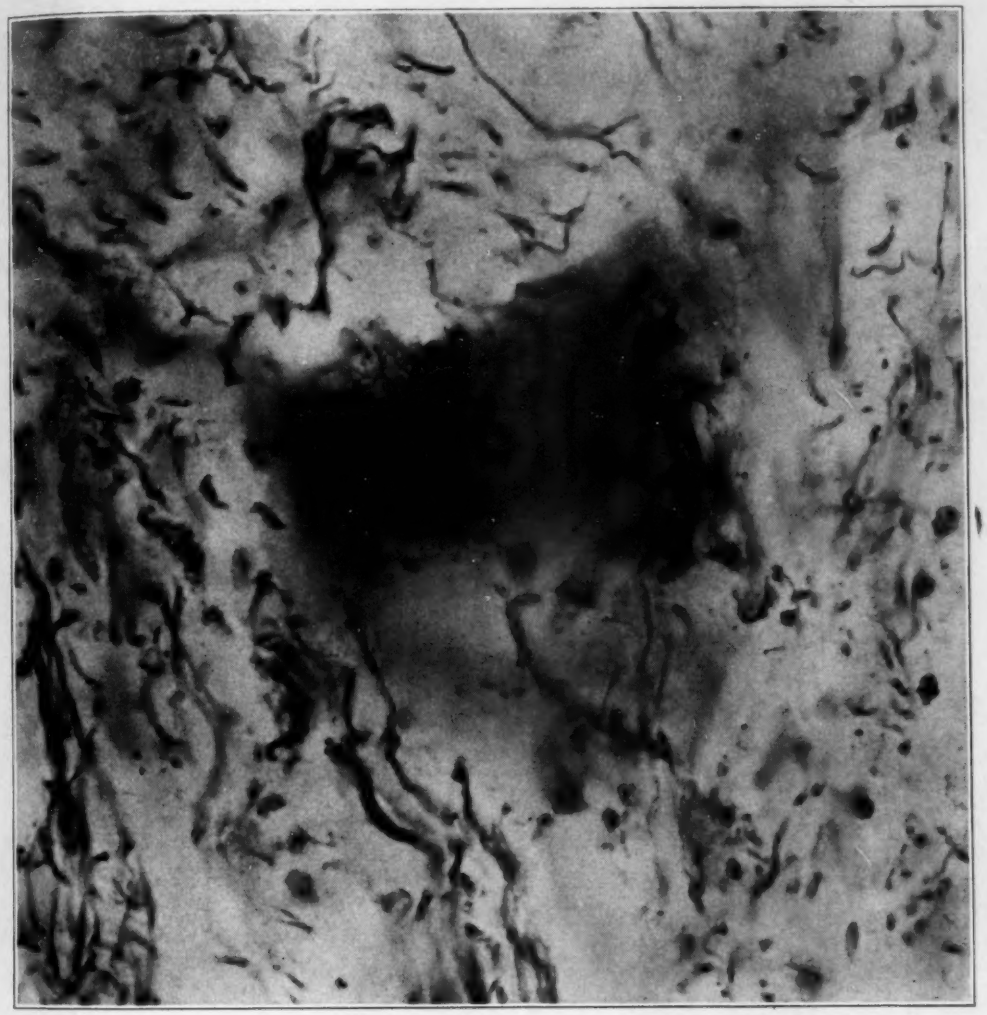

Fig. 4.—Elongated *boutons* which have degenerated over a period of seventy-two hours. These spatula-like structures stand out against the cell background. The former circular configuration has disappeared. Magnification: 2,900 diameters.

The seventy-two hour stage proved to be one of the most interesting, both in shape and in size (fig. 4). The transformation from a disk to a spatula-like shape resulted in a noticeable increase in length and area.

This transition was usually sharp and afforded unmistakable evidence of degeneration. The *bouton* at this stage still preserved the homogeneity of structure and stain already seen in the earlier stages.

Fig. 5.—Anterior horn cell of a cat killed ninety-six hours after section of the spinal cord. The photograph shows a normal *bouton* adjacent to the greatly enlarged degenerated ending. Magnification: 2,900 diameters.

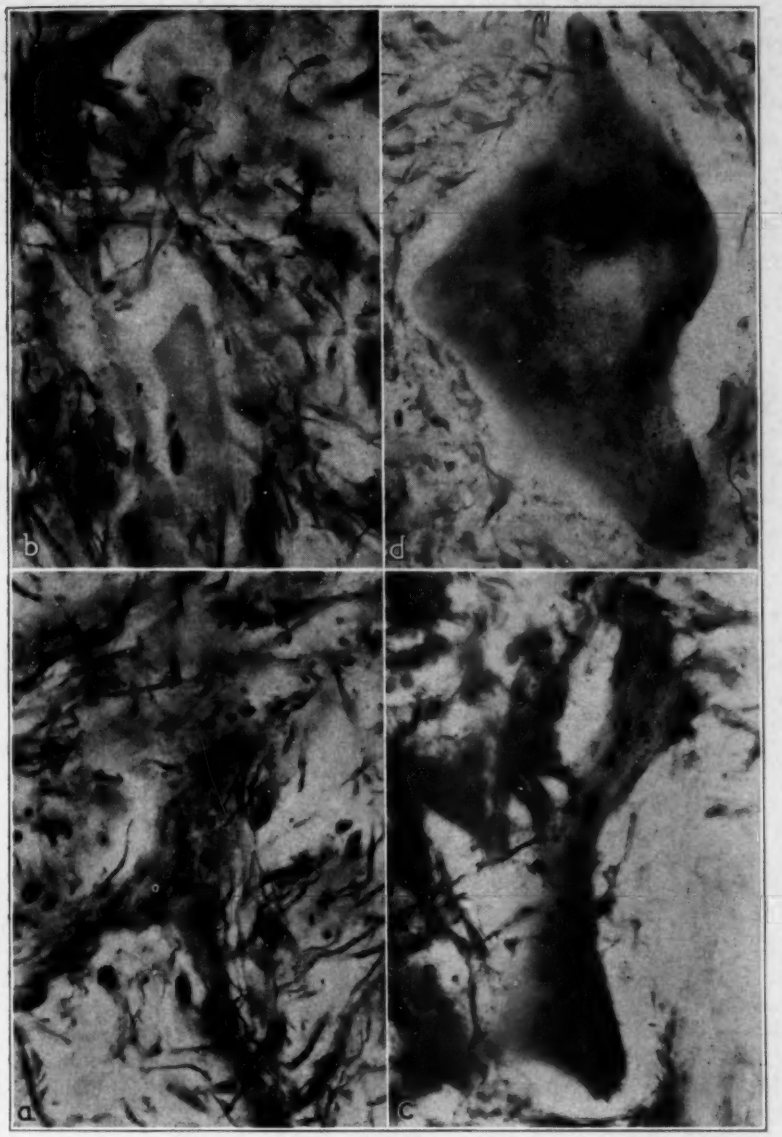

Fig. 6.—Final stages in the degeneration of *boutons terminaux* one hundred and twenty hours after section of the spinal cord. In *a* is a greatly enlarged granular *bouton* at one edge of the cell. In *b* is shown fragmentation of some of the *boutons* about two anterior cells. In *c* the *boutons* have broken up into quite sharp, discrete granules, present both at the periphery of the nerve cell and on its surface. In *d* are seen granular smudges on the surface of the nerve cell about which all *boutons* have degenerated. These are the only traces left of the *boutons* and depict most clearly the terminal stage of disintegration.

In ninety-six hours the *bouton* had become granular and increased in length and width (fig. 5). The relatively smooth contour was disrupted by large granules that were ready to break away. This was the last stage in which it could be said that the *bouton* was an intact structure.

The changes seen after one hundred and twenty hours varied within rather wide limits, depending on the location of the cell studied relative to the section of the cord. The characteristic of this stage was fragmentation of the formerly solid black mass. In some *boutons* (fig. 6 *a*)

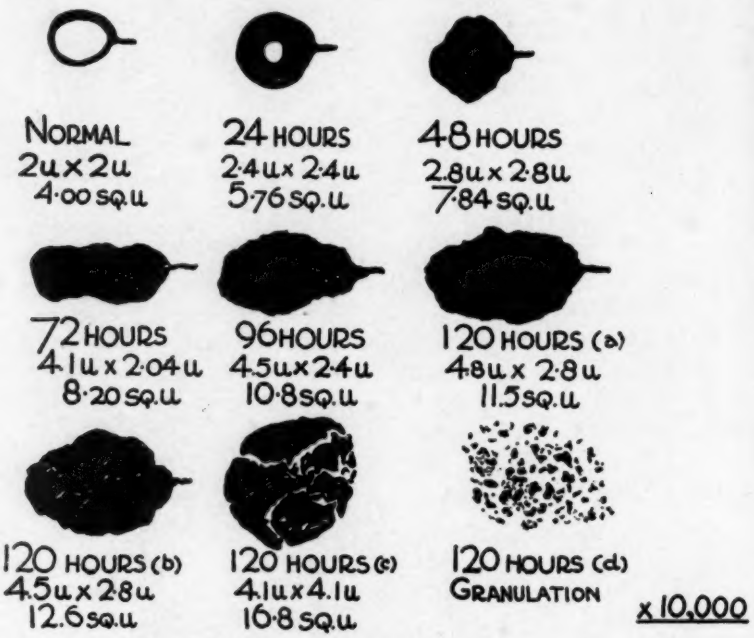

Fig. 7.—Diagrammatic drawing to show the stages of *bouton* degeneration. The transition in shape from the circular to the ellipsoid and back to the circular can be seen. Measurements of the cells from which these sketches were made are given in each case, together with the approximate area. Degenerative changes in the *bouton* are most marked between the periods of seventy-two and ninety-six hours. Magnification: 10,000 diameters.

only the periphery had begun to break up, while in others (fig. 6 *b*) clefts could be seen in the central part. More advanced still were the phases in which the body was completely disrupted. There was a considerable tendency again toward the circular shape, although the increased diameter could be attributed partly to the interstices between the segments (fig. 6 *c*).

Finally, there occurred the familiar granular disintegration and total fragmentation of these structures (fig. 6 *d*). In a few cases the semblance in shape to a *bouton* could be seen, but usually the granules were more widely dispersed and not easily recognizable.

As can be seen in figure 7, an average degenerating *bouton* passes through the processes of hypertrophy, elongation, fragmentation and granulation, and from the circular to the ellipsoid and back to the circular again.

COMMENT

It should be stated clearly that the *bouton* method is a silver method and is subject to the vagaries of all types of silver staining. It is reasonable to suppose that the *boutons terminaux* undergo the changes described whenever their axon is interrupted. It would be unfair, however, to assume that because abnormal *boutons* were not stained by the silver technic, no degenerative changes had taken place. In most cases it is impossible to stain more than a small proportion of the degenerated *boutons* around a cell, but those which do appear are usually well defined.

The interpretation of the present work is based on the assumptions (*a*) that *boutons terminaux* occurring in the dorsal, ventral and lateral horns are normally of the same size and (*b*) that terminal arborizations of an axis-cylinder degenerate in one and the same manner, regardless of the finer architecture of their axon or the location of their cell of origin, whether it is a pyramidal or an intercalated cell.

CONCLUSION

The degenerative changes noted in the *boutons terminaux* are in accord with the accepted observations on neurofibrillar degeneration in the peripheral segments of sectioned nerves.

The optimum period of degeneration of the *boutons* in the spinal cord, from the points of view of ease and certainty of recognition, is from seventy-two to ninety-six hours.

Criteria for determination of the length of time which a *bouton* has been degenerating have been set forth in order that the technic may be more widely applied, especially in cases in which it is desired to differentiate between *boutons* of longer and those of shorter periods of degeneration.

FACTORS PRODUCING LUMBAR CEREBROSPINAL FLUID PRESSURE IN MAN IN THE ERECT POSTURE

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It is our purpose to determine which of the elastic components of the craniovertebral system of man is responsible for the lumbar cerebrospinal fluid pressure when the subject is in the sitting position.

THE CRANIOVERTEBRAL SYSTEM

The craniovertebral system of man (fig. 1) is composed of the bony and ligamentous elements of the cranial and vertebral cavities, together with the brain and spinal cord, the cerebrospinal fluid, the meninges and the vascular tree enclosed within these cavities. This system therefore contains certain elements capable of changes of volume and pressure. The outer envelop of the system is obviously not rigid, for alterations in pressure may be transmitted to the cerebrospinal fluid via the systemic veins during respiration and during abdominal or jugular compression. Furthermore, on change from the recumbent to the erect position with the head up or down, added volumes of cerebrospinal fluid are displaced from the system into a lumbar or cisternal open end manometer. A rigid container, closed at the top and less than 34 feet (11 meters) high, would not permit displacement of cerebrospinal fluid from it on change of position. Therefore, the craniovertebral system is not rigid. On the other hand, the system is not entirely exposed to atmospheric pressure, for it will support subatmospheric pressures existing normally at and above the cisterna magna when the subject is in the erect position with the head up, as

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* Dr. Carmichael was working on behalf of the Medical Research Council, Great Britain.

This work was carried out at the Research Unit, the National Hospital, Queen Square, London, while Dr. von Storch held a Rockefeller Foundation Fellowship, and at the Department of Neurology, the Harvard University Medical School, and the Neurological Unit, the Boston City Hospital.

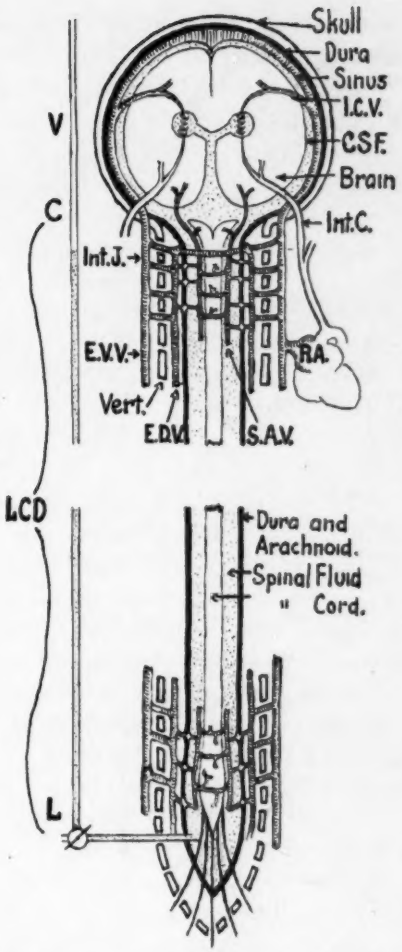

Fig. 1.—Diagram of the craniovertebral system. *Int. C.* indicates the internal carotid artery; *Int. J.*, the internal jugular vein, and *E. V. V.*, the extravertebral veins anastomosing through the vertebra *(Vert.)* with the extradural veins *(E. D. V.)*, which in turn anastomose through the dura with the subarachnoid veins *(S. A. V.)*. *R. A.* indicates the right auricle, the "outlet" of the venous system. *I. C. V.* is an intracranial vein emptying into the internal jugular vein, but not in direct hydrodynamic continuity with the subarachnoid vertebral veins. Note that the extravertebral veins form with the subarachnoid veins a continuous lattice transmitting alterations of venous pressure to the cerebrospinal fluid *(C. S. F.)*.

V, *C* and *L* represent the ventricular, cisternal and lumbar cerebrospinal fluid pressures with the subject in the sitting position. Note that the vertical lumbo-cisternal distance *(L C D)*, expressed in millimeters, closely approximates the observed lumbar cerebrospinal fluid pressure, registered in millimeters of water (or cerebrospinal fluid).

The arachnoid is considered as applied to the veins and the dura and is therefore omitted from the diagram. The rigid arterial tree is likewise omitted.

well as those resulting from extraction of cerebrospinal fluid when the subject is in the recumbent position. Therefore, the craniovertebral system of man is semirigid and hence must contain elastic elements.

The factors which may vary the cerebrospinal fluid pressure in the recumbent position are: arterial, arteriolar and capillary blood pressure; filtration, dialysis, osmosis and selective secretion of the choroid plexus, and volume of the central nervous system and of the cerebrospinal fluid. None of these factors alter rapidly during a change of posture. The remaining factors are: pressures in the intracranial venules, veins, sinuses and systemic veins; dural and arachnoid elasticity, and alterations in the vertebral epidural space. The relatively rigid sinus walls are not likely to transmit significant changes in pressure to the cerebrospinal fluid. Their thick walls are continuous with the relatively thin walls of the veins and venules. Transmission of pressure, which implies capability of movement of the intervening wall, would occur more readily along the course of the veins and venules. Systemic venous pressure may be transmitted to the veins (and capillaries) within the craniovertebral system, and thence to the cerebrospinal fluid. This becomes evident during respiration and compression of the abdominal or jugular veins. On the other hand, it is doubtful whether the cerebrospinal fluid pressure influences the systemic venous pressure as long as cardiac compensation is adequate.

Dural elasticity within the cranium is negligible because of the adherence of the dura to the inner table of the calvarium. The intravertebral dura, however, may be capable of collapse or expansion subsequent to changes in intradural and extradural pressure, but because of the nonelastic character of the dura, expansion is probably minimal. Owing to the intimate attachment of the dura to the vertebrae in the upper cervical region, collapse in that location is unlikely. Changes in the normally subatmospheric epidural pressure are probably secondary to intradural and intravascular changes, as well as to curvature of the spine. This aspect of the problem will be dealt with in a subsequent report.

Thus, the elastic elements of the craniovertebral system concerned with the erect posture are: (1) venous alteration, i. e., possible expansion of (*a*) intracranial veins and (*b*) intradural lumbar veins, and (2) dural alterations, i. e., (*a*) possible (cervical?) collapse and (*b*) possible lumbar expansion.

Weed [1] has shown in animals that the use of an open end manometer of 2 mm. bore, allowing displacement of cerebrospinal fluid into it,

1. Weed, L. H.: Positional Adjustments of the Pressure of the Cerebrospinal Fluid, Physiol. Rev. **13**:80 (Jan.) 1933.

registers the cerebrospinal fluid pressure with but slightly less accuracy than a nondisplacement manometer. In man, with a larger cerebrospinal fluid reservoir, this discrepancy is even further diminished. It must be remembered, however, that cerebrospinal fluid is displaced in such a manometer and is then interpreted as pressure.[2] The height of the column of fluid in the manometer is a measure of the pressure subsequent to displacement of the fluid. In a manometer of 2 mm. bore, 0.3 cc. of cerebrospinal fluid is displaced for every 100 mm. of pressure registered; that is, a change in volume of about 0.9 cc. occurs during postural alteration (from the recumbent to the sitting position). Therefore an almost imperceptible alteration occurs in the entire volume of the craniovertebral system. In an erect, rigid container, closed at the top, less than 34 feet (11 meters) in height and completely filled with fluid of a specific gravity of 1.008, the pressure at the bottom will be increased by the height of the column, but no fluid will be displaced. Hence, the pressure is not measurable by the usual displacement methods. Thus, the measurable effect of the column of cerebrospinal fluid is wholly dependent on the elastic factors listed.

REVIEW OF THE LITERATURE

In recent years Weed, working with Flexner and others,[3] demonstrated that the postural alterations observed in the cerebrospinal fluid pressure of dogs, cats, macaques and chimpanzees are due to several elastic elements which modify the rigidity of the craniovertebral box. These components are: (1) latent hydrostatic effect of the column of cerebrospinal fluid, (2) reflection of the venous pressure on this column and (3) meningeal elasticity, determined by the capacity of the vertebral dura to collapse. These investigators concluded that about 63 per cent of the venous pressure is reflected on the cerebrospinal fluid pressure and that this percentage of reflection determines entirely the cerebrospinal fluid pressure in the vertical head-down position. They

2. Pressure expressed in the usual clinical units is the force per unit area which will support against atmospheric pressure a column of so many millimeters of water, saline solution or cerebrospinal fluid. For example, a pressure of 136 mm. of cerebrospinal fluid equals 10 mm. of mercury more than atmospheric pressure, or a total of 770 mm. of mercury; or a pressure of 136 mm. of cerebrospinal fluid is 0.19 pound (86 Gm.) per square inch (6.5 cm.) above atmospheric pressure.

3. Weed, L. H., and Flexner, L. B.: Cerebrospinal Elasticity in the Cat and Macaque, Am. J. Physiol. **101**:668 (Sept.) 1932; The Relations of the Intracranial Pressures, ibid. **105**:266 (Aug.) 1933. Flexner, L. B., and Weed, L. H.: Factors Concerned in Positional Alterations of Intracranial Pressure, ibid. **104**: 681 (June) 1933; Note on the Cerebrospinal Elasticity in a Chimpanzee, ibid. **105**:571 (Sept.) 1933. Weed.[1]

concluded that the cerebrospinal fluid pressure in the vertical head-up position is determined by the meningeal element and that the vascular element is latent. After they had determined by direct measurement of the elasticity of the excised dura that its potential expansion is negligible, they concluded that in the erect position the meningeal factor is determined solely by collapse of the cervical dura (fig. 5 *B*). Thus, they expressed the belief that the lumbar cerebrospinal fluid pressure in the erect posture is determined by the degree of potential collapse of the cervical dura. These authors did not state that their observations were strictly applicable to man. It has, however, been the tendency of other investigators to apply these results to man.

Duane, Lewis and Ravdin,[4] by rotating animals about the craniolumbar axis, demonstrated that the position of the heart and its relation to the venous pressure influence directly the cerebrospinal fluid pressure in the recumbent position.

Masserman,[5] in investigations on man, showed that rapid removal of cerebrospinal fluid causes edema and vascular engorgement of the neuraxis, thus decreasing the ventriculosubarachnoid space. The slow removal of cerebrospinal fluid was shown not to alter the volume of the ventricles and the subarachnoid space or the total elasticity of the system. Masserman observed that the mean lumbar cerebrospinal fluid pressure in the sitting position was 432 mm., which was less than the distance between the point of puncture and the vertex of the skull.

Myerson, working with Loman and others,[6] demonstrated in man that the position of the heart relative to the cerebrospinal fluid axis actively influences the cerebrospinal fluid pressure when the subject is in the lateral recumbent, supine, "hands and knees," head-up and head-down positions. Their results suggest that, as the venous pressure is altered by posture, the alteration of cerebrospinal fluid pressure due to posture is a reflection of the venous pressure. They observed that there is no relationship between the lumbar cerebrospinal fluid pressure measured in the recumbent and that measured in the erect sitting position. They also determined that the lumbar cerebrospinal fluid pressure in the

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4. Duane, W.; Lewis, R. M., and Ravdin, I. S.: Cerebrospinal Fluid Pressure During Alterations in Posture, Arch. Neurol. & Psychiat. **24**:1291 (Dec.) 1930.

5. Masserman, J. H.: Cerebrospinal Hydrodynamics: Clinical Experimental Studies, Arch. Neurol. & Psychiat. **32**:523 (Sept.) 1934; Cerebrospinal Hydrodynamics: Studies of the Volume Elasticity of the Human Ventriculo-Subarachnoid System, J. Comp. Neurol. **61**:543 (June 15) 1935.

6. (*a*) Myerson, A., and Loman, J.: Internal Jugular Venous Pressure in Man: Its Relationship to Cerebrospinal Fluid and Carotid Arterial Pressures, Arch. Neurol. & Psychiat. **27**:836 (April) 1932. (*b*) Loman, J.; Myerson, A., and Goldman, D.: Effects of Alterations in Posture on the Cerebrospinal Fluid Pressure, ibid. **33**:1279 (June) 1935.

sitting position is approximately equal to the vertical distance from the lumbar needle to the cisterna magna. They suggested that the lumbar cerebrospinal fluid pressure in man in the erect position is a direct reflection of the venous pressure at that level. No direct evidence of this was presented.

METHODS

The effect of postural alteration was investigated by various methods in a series of 170 patients. All subjects were excluded in whom there was any evidence of intravertebral or intracranial neoplasm, abnormalities of volume or consistency of the cerebrospinal fluid or cardiovascular disease. Some patients were aided in changing from the recumbent to the sitting position by a combined chair and table used for encephalography.[7] The rest were placed in the right lateral recumbent position on a tilting table. This table was equipped with straps, so that the patient could be tilted to the sitting or to the head-down position without changing the original attitude. Lumbar and cisternal punctures were performed with the usual aseptic technic, needles with an attached three way stopcock being used. Pressures were measured with open end manometers of 2 mm. bore attached directly to the needles. As has been shown, these manometers measure the pressure within the limits of experimental error. Readings were not corrected for surface tension (15 mm. of water). When rubber tubing was used between the manometer and the needle, it was filled with sterile saline solution before the measurement of pressures. In recording cisternal pressures U-shaped manometers were used. Pressure was recorded in the usual clinical units—millimeters of cerebrospinal fluid.

RESULTS

1. *Lumbar Cerebrospinal Fluid Pressure in the Sitting Position.*—One of us (von Storch[8]) reported the relationship existing between the lumbar cerebrospinal fluid pressure in the recumbent and that in the sitting position and correlated the latter with the lumbocisternal distance. These observations have been combined with the present series. It was demonstrated in 145 patients that the initial lumbar cerebrospinal fluid pressure normal for any person in the recumbent position bears no direct relationship to the pressure for that person in the sitting position (fig. 2).

It was observed in a series of 101 patients that the lumbar cerebrospinal fluid pressure in the sitting position is roughly equivalent to the distance between the point of puncture and the cisterna magna (figs. 3 and 4). This relationship was closer in the present series of normal persons than in the earlier series of anesthetized and narcotized patients. These observations confirm those of Myerson and Loman.[6a]

7. Epstein, S. H., and von Storch, T. J. C.: Improved Apparatus for Encephalography Adaptable to Ventriculography, Am. J. Roentgenol. **34**:451 (Oct.) 1935.

8. von Storch, T. J. C.: Clinical Application of the Craniovertebral Dynamics to Encephalography, Brain **59**:250 (June) 1936.

2. Effect of Intracranial Venous Engorgement on the Lumbar Cerebrospinal Fluid Pressure in the Sitting Position (fig. 5 *C*).—In 10 patients the lumbar cerebrospinal fluid pressure was measured with the subjects in the lateral recumbent position. After the usual dynamic tests had demonstrated continuity of the column of fluid, the patients were tilted to the erect sitting position, and measurements were made of the lumbar cerebrospinal fluid pressure and the vertical lumbocisternal

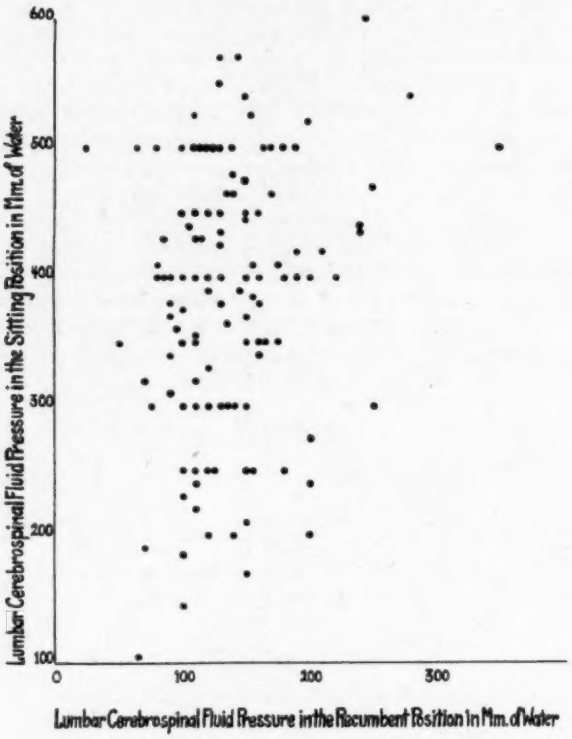

Fig. 2.—Relationship of the normal lumbar cerebrospinal fluid pressure in the sitting and that in the recumbent position in the same subject (145 cases).

Each dot represents the normal pressure with the subject in the recumbent position (abscissa) plotted against the normal pressure for the same person in the sitting position (ordinate), when measured within two minutes. Note that with low pressures in the recumbent position either low or high pressures in the sitting position may occur, and vice versa. There is normally no direct relationship between the pressures in the two positions.

distance. The patients were then returned to the recumbent position, and the cerebrospinal fluid pressure was increased and maintained by varying degrees of unilateral and bilateral jugular compression. The

patients were again tilted into the erect position, the jugular compression being maintained during the tilting. Thus, the cerebrospinal fluid pressure in the sitting position was compared with various levels of the cerebrospinal fluid pressure in the recumbent posture.

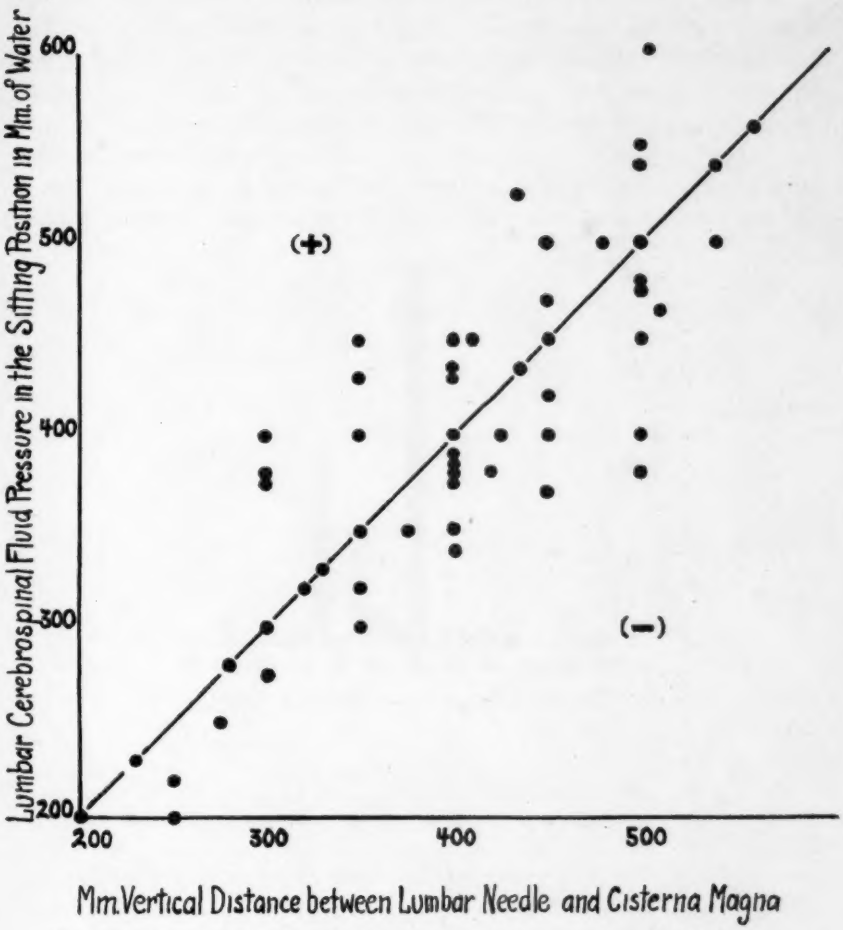

Fig. 3.—Range of relationship between the lumbar cerebrospinal fluid pressure observed normally with the subject in the sitting position and the vertical lumbocisternal distance for that patient (101 cases).

Each dot represents values for several persons (see figure 4), those falling on the line indicating equality between the pressure in the sitting position and the lumbocisternal distance. Note that there is a tendency to preserve this equality with varying lengths of the back.

It was demonstrated that when the cerebrospinal fluid pressure in the recumbent position was increased by intracranial venous engorgement the pressure in the sitting position was increased by a like incre-

ment, within the limits of experimental error (fig. 6). Therefore variable engorgement of the intracranial venous bed, which altered its potential distensibility, did not change the response of the system to the erect posture.

3. *Effect of Subarachnoid Lumbar Venous Engorgement on the Lumbar Cerebrospinal Fluid Pressure in the Sitting Position* (fig. 5 *D*). —In a group of 5 patients the same technic was employed, except that the cerebrospinal fluid pressure was increased by manual abdominal compression. This compression was maintained during tilting and while the patient was erect. The results in all experiments were identical. Increasing the lumbar cerebrospinal fluid pressure in such a fashion did not result in significant alteration of the pressure normally present

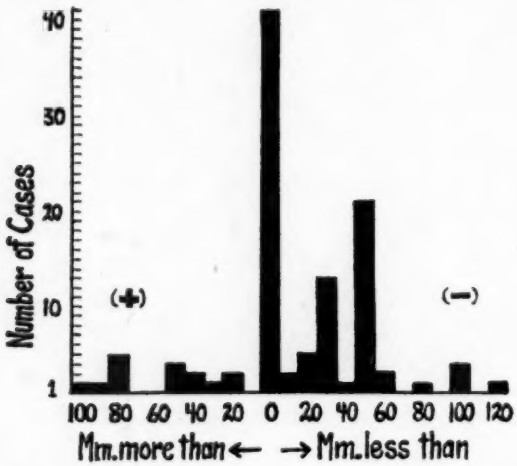

Fig. 4.—Relationship between the vertical lumbocisternal distance and the lumbar cerebrospinal fluid pressure in the sitting position (101 cases).

The abscissa denotes the number of millimeters by which the pressure in the sitting position exceeded (+) or was less than (—) the vertical lumbocisternal distance. Note that in the majority of cases (40) these factors are equal. In a large number of cases the pressure may be slightly (from 20 to 50 mm.) less than the distance.

in the sitting position (fig. 7). The pressure in the erect position was thus the same with or without abdominal compression.

4. *Effect of a Complete Spinal Subarachnoid Block on Lumbar Cerebrospinal Fluid Pressure in the Sitting Position* (fig. 5 *E*).—Tilting experiments were carried out with 3 patients in whom an intravertebral neoplasm had been diagnosed clinically and dynamic tests had demonstrated a complete subarachnoid block. The existence of the block was confirmed by the presence of the normal response to abdominal compression in the absence of any response to bilateral jugular com-

pression, and later by operation. After the tests the patient was tilted to the sitting position, and measurements were made of the lumbar cerebrospinal fluid pressure, the vertical lumbocisternal distance and the distance between the lumbar needle and the clinical level of the block.

Observations in these experiments showed that the lumbar cerebrospinal fluid pressure increased until the column of cerebrospinal fluid in the manometer was about equal to the lumbocisternal distance. The meniscus of the fluid in the manometer thus rose above the clinical level of the spinal block. Response to increased abdominal tension was the same as that in the normal patient (fig. 8).

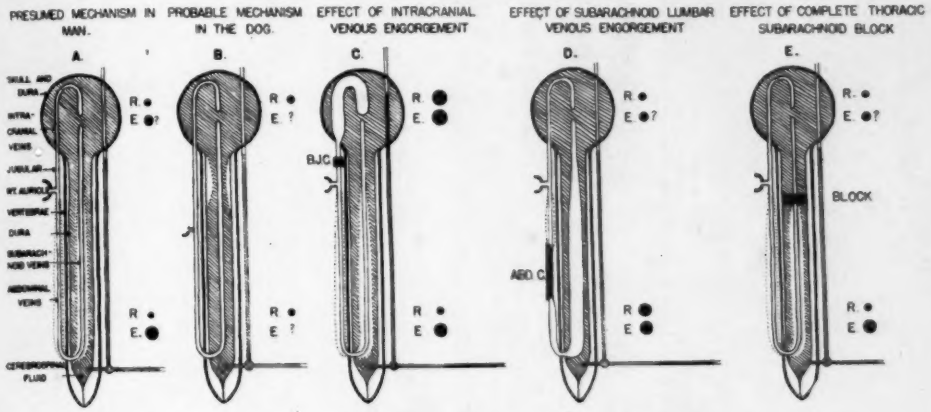

Fig. 5.—Mechanism producing the lumbar cerebrospinal fluid pressure when the subject is in the erect (sitting) position.

All changes in volume are grossly exaggerated. The central nervous system and the inelastic arterial system are omitted. By turning the diagrams on their left sides the recumbent position is simulated, and pressures may be read from the small manometers. Dotted lines denote alteration of dural (*B*) or venous walls on assumption of the erect position. The circles following *R* and *E* in the cranial and lumbar regions portray the cranial and the lumbar venous volumes when the subject is in the recumbent (*R*) and in the erect (*E*) position, respectively. *B.J.C.* denotes bilateral jugular compression applied in the recumbent position and maintained in the erect position. *ABD.C.* denotes abdominal compression applied in the same manner. Striped levels in the lumbar manometers indicate the normal levels of the lumbar cerebrospinal fluid pressure in the recumbent position (small manometer) and in the erect position (large manometer). Solid black levels in the manometers indicate the pressure levels due to bilateral jugular or abdominal compression. In the dog (*B*) the heart is situated more nearly halfway between the lumbar region and the vertex.

Note that the lumbar cerebrospinal fluid pressure normally approximates the vertical distance between the needle and the cisterna magna. This pressure is unaffected by complete subarachnoid block (*E*). Note also that increase in the cerebrospinal fluid pressure due to intracranial venous engorgement (*C*) is a component of the pressure in the sitting position, whereas that due to lumbar venous engorgement (*D*) is not.

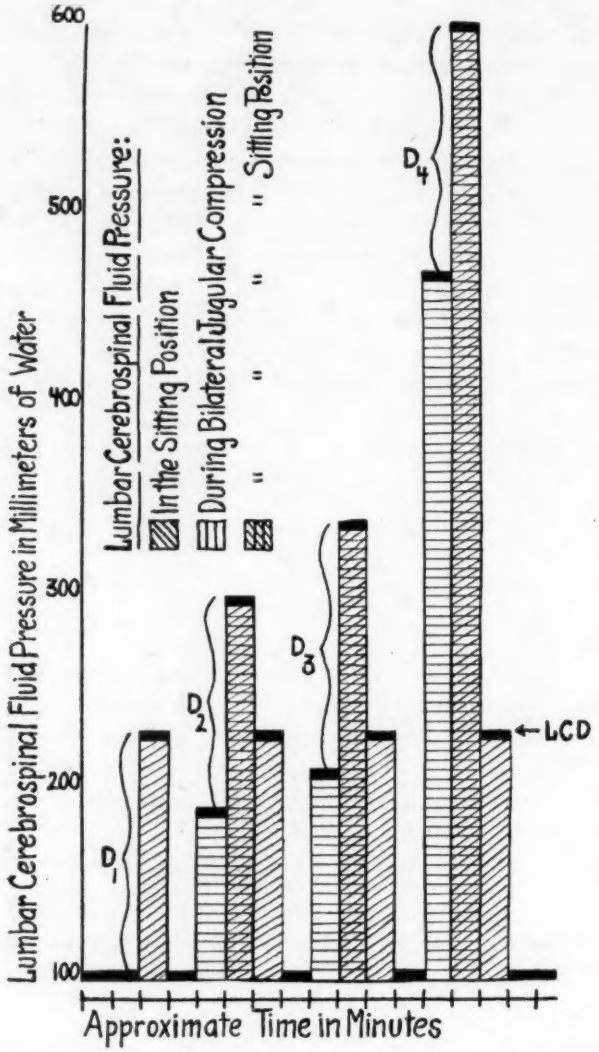

Fig. 6.—Effect of increased intracranial venous pressure on the lumbar cerebrospinal fluid pressure in the sitting position.

The figure illustrates the observations in a typical experiment. The heavy lines indicate the pressure levels of the lumbar cerebrospinal fluid (100 mm. of water with the subject in the recumbent position) subsequent to bilateral jugular compression, assumption of the sitting position and bilateral jugular compression initiated in the recumbent position but maintained during the sitting position. The level LCD (230 mm.) indicates the level of the cisterna magna, that is, the vertical distance from the lumbar puncture to the cisterna magna. Note that the pressure in the sitting position equals this distance and that the difference in the pressures in the recumbent and in the sitting position (D_1, D_2, D_3, D_4) tend to remain constant despite the increases in the level of the "recumbent pressure" produced by intracranial venous engorgement.

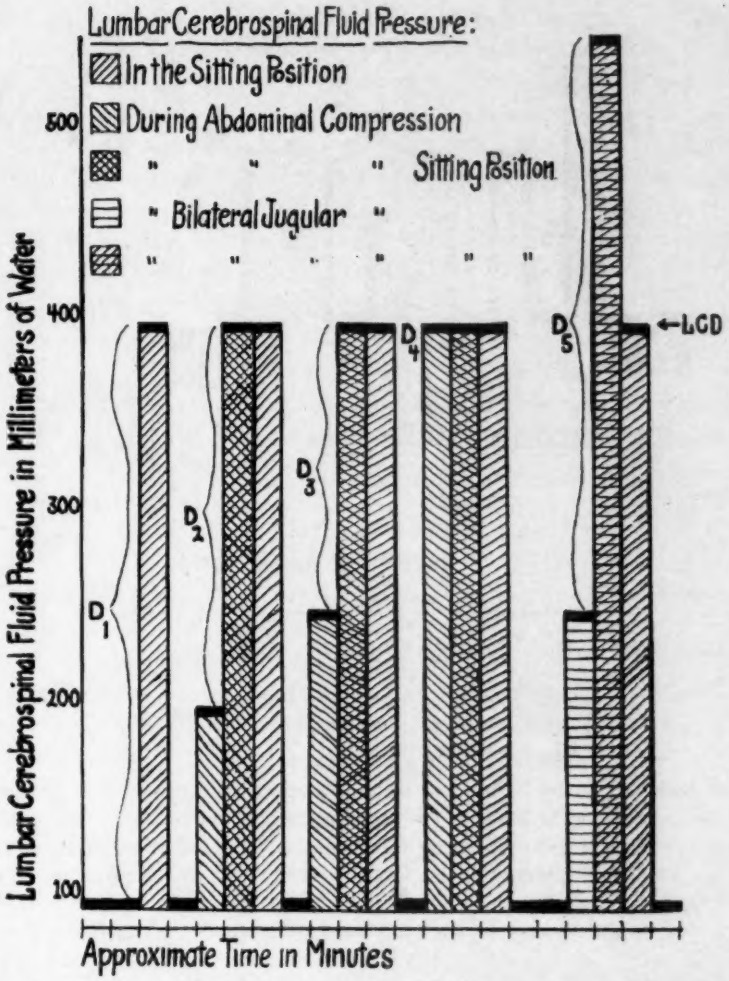

Fig. 7.—Effect of increased lumbar subarachnoid venous pressure on the lumbar cerebrospinal fluid pressure in the sitting position, as compared with the effect of increased intracranial venous pressure.

The figure illustrates the observations in a typical experiment. The heavy lines indicate the level of the lumbar cerebrospinal fluid pressure (100 mm. of water in the recumbent position) subsequent to abdominal compression, bilateral jugular compression, assumption of the sitting position or any of these forms of compression combined with the sitting position. LCD indicates the level of the cisterna magna with respect to that of the lumbar puncture, that is, 400 mm. above the lumbar puncture in this case. Note that the pressure in the sitting position equals this distance. The difference between the pressures in the recumbent and those in the sitting position (D_1, D_2, D_3 and D_4) progressively decreases as increased abdominal compression is applied, but jugular compression does not alter this difference (D_1 and D_5). See also figure 6.

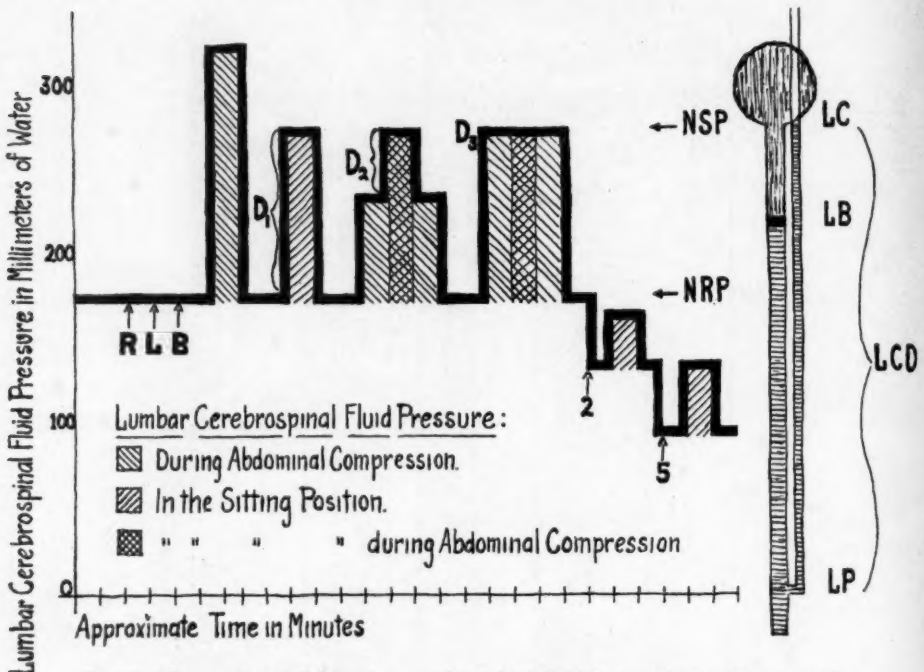

Fig. 8.—Dynamics of the lumbar cerebrospinal fluid in a patient with a complete subarachnoid block at the level of the fourth thoracic vertebra.

The continuous line represents alterations in pressure of the lumbar cerebrospinal fluid. *R, L* and *B* indicate the application of compression in the right, left and both jugular veins with the patient in the recumbent position. The numerals *2* and *5* indicate withdrawal of 2 and 5 cc. of spinal fluid respectively, from the lumbar sac. *NRP* indicates the level of lumbar cerebrospinal fluid pressure (180 mm. of water) which is normal for this patient in the recumbent position. *NSP* indicates the level of lumbar cerebrospinal fluid pressure (280 mm. of water) which is normal for this patient in the sitting position. At the right is a diagram of the patient with manometer attached, in which *LP* indicates the level of puncture, *LB* the level of the block (220 mm. above the puncture), *LC* the level of the cisterna magna (280 mm. above the puncture) and *LCD* the vertical lumbocisternal distance. Note that with the patient sitting erect the lumbar cerebrospinal fluid pressure is normal, although the block excludes factors above it, such as collapse of the cervical dura; that it is greater than can be accounted for by the column of cerebrospinal fluid below the block, and that it reacts normally on abdominal compression (the differences between pressures in the recumbent and those in the sitting position, D_1, D_2 and D_3 progressively decrease). Note also that removal of even very small volumes of cerebrospinal fluid grossly distorts the normal dynamic responses.

Several other observations of importance were made in evaluating the results. Loss of even a small amount of cerebrospinal fluid from the comparatively small subarachnoid space below the block diminished the usual increase of the lumbar cerebrospinal fluid pressure when the patient was in the erect position—much more than would the loss of an equal amount of fluid in a normal person. Abdominal compression produced a greater response than normal, and anxiety or bodily tension was readily reflected on the cerebrospinal fluid pressure through increased venous tension. It is possible in the latter circumstance for the meniscus of cerebrospinal fluid in the manometer to pass above the level of the spinal block.

COMMENT

It has been observed [6] that the lumbar cerebrospinal fluid pressure in the sitting position is equal to that in the erect standing position. As the column of cerebrospinal fluid is continuous from the upper part of the sacrum to the vertex of the cranium, pressures measured at the lumbar region may be used to compute intracranial pressures.

The present observations have demonstrated that in man the normal lumbar cerebrospinal fluid pressure in the sitting position bears no relationship to the normal pressure for that person in the recumbent position. Therefore, the lumbar cerebrospinal fluid pressure in the sitting position cannot be calculated by any multiple of, or by the addition of any arbitrary sum to, the pressure in the recumbent position. It was demonstrated that only a fraction of the potential gravitational effect of the column of cerebrospinal fluid from the vertex to the needle is demonstrable in the lumbar cerebrospinal fluid pressure in the sitting position. The lumbar cerebrospinal fluid pressure in the sitting position was found to be roughly equivalent to the vertical distance between the cisterna magna and the point of puncture. Therefore, it cannot be calculated as the sum of this distance and the pressure in the recumbent position. An estimate of the lumbar cerebrospinal fluid pressure in the sitting, and hence in the erect, position may be made by considering it to be equivalent to the vertical lumbocisternal distance. Any further degree of accuracy requires direct measurement in a relaxed subject.

In a series of unpublished observations at the National Hospital, E. Graeme Robertson has demonstrated that the lumbar cerebrospinal fluid pressure of man with the head down averages 65 mm. of water more than atmospheric pressure. Weed's [3] observations on dogs have demonstrated that this pressure is subatmospheric with the head in the same position. It is therefore suggested that the postural alterations of cerebrospinal fluid pressure in man and those in the dog may be due to different mechanisms.

In the following discussion and in referring to figure 5 it must be remembered that alteration of venous volume is actually slight (a change in volume of 0.9 cc. for the entire craniovertebral venous system) and has been exaggerated in the discussion and the diagrams merely to illustrate that such alteration occurs.

In the present group of experiments it was shown that an increase in the lumbar cerebrospinal fluid pressure in the recumbent position due to jugular compression did not alter the normal increase in pressure on assumption of the erect posture (figs. 5 *C*, and 6). Thus, the usual increase in cerebrospinal fluid pressure due to postural change was merely superimposed on the higher level of pressure in the recumbent position. Therefore the elastic factor responsible for the observed postural change in pressure remained unaltered. As jugular compression increased the intracranial venous pressure by engorgement of the intracranial veins, the potential expansibility of these veins must have been greatly decreased by this engorgement. Therefore, as alterations in the potential elasticity of the intracranial veins failed to alter the elasticity of the total system, it follows that these veins are only secondarily concerned with the cerebrospinal fluid pressure observed in the erect position.

When the lumbar cerebrospinal fluid pressure in the recumbent position was increased by abdominal compression very different results were obtained. It was observed that the pressure in the erect position during abdominal compression was the same as without such compression (figs. 5 *D* and 7). Hence, the increase in pressure observed on tilting the patient to the erect position decreased as the pressure in the recumbent position was increased. The higher level of lumbar cerebrospinal fluid pressure in the recumbent position was produced by increase in the venous pressure within the intradural lumbar veins. Owing to the elasticity of the veins, pressure was transmitted to the cerebrospinal fluid when these veins became engorged. On changing the patient to the erect position, the pressure within these veins was increased to a new and higher level by the column of venous blood above the lumbar level. In the normal subject in the erect posture the lumbar veins are distended to their normal maximum when a displacement manometer is attached. Abdominal compression when the subject is in the recumbent position produces partial distention, and when the patient is erect the veins again distend to their normal maximum. Thus, the increase in pressure on changing from the recumbent to the erect posture is less with than without lumbar compression. Therefore, alteration of abdominal venous distention alters the elastic response of the system to the erect posture.

There remains only the question of elasticity of the vertebral dura. This effect might be due to collapse of the upper and expansion of the

lower parts of the dura. Weed's [3] observations in dogs led him to conclude that the lumbar cerebrospinal fluid pressure in the erect position is due to collapse of the cervical dura, allowing displacement of cerebrospinal fluid into a manometer (fig. 5 *B*). In the present series of experiments on man involving abdominal and jugular compression, the increases of cerebrospinal fluid pressure in the recumbent position, however produced, acted on the dura in the same fashion. The increased intradural pressure must have tended to expand the dura in its upper and lower segments. Its effect on displacement of cerebrospinal fluid into a manometer when the patient is erect must therefore have been in the same direction in both sets of experiments, for the dural changes were the same in each case. The results in the two groups of observations were, however, diametrically opposed. Therefore, it is improbable that the dural elasticity can be the determining factor in the production of the lumbar cerebrospinal fluid pressure observed in the erect position.

The experiments on patients with complete spinal subarachnoid block confirmed the conclusions derived from the former experiments. Therefore, changes in volume and pressure in the intracranial venous bed do not affect the lumbar cerebrospinal fluid pressure with the subject in the erect position, thus confirming the experiments on jugular compression. We have demonstrated that in man a block below the cervical area failed to alter the lumbar cerebrospinal fluid pressure, and therefore possible collapse of the cervical dura is merely a secondary factor (fig. 5 *E*).

The only component which remains unaltered by complete subarachnoid block is the effect of the column of venous blood. The intradural veins in man communicate segmentally with the vertebral column and the extravertebral veins (fig. 1). There is a continuous valveless column to the right auricle which would not be interrupted by an intravertebral mass. Thus, the normal changes in intradural lumbar venous pressure would occur during changes in posture. Therefore, reflection of the intradural intravenous pressure is the only factor which could produce normal lumber cerebrospinal fluid pressure in the presence of a complete subarachnoid block.

It may now be concluded that the lumbar cerebrospinal fluid pressure in man measured in the sitting (or erect) position is determined by the intradural venous pressure existing at the lumbar level (fig. 5 *A*). This venous pressure is determined by the hydrostatic effect of the column of blood below the right auricle, the pressure existing within the right auricle and the rate of flow of the blood. Since the difference in pressure responsible for the rate of flow is very small, the lumbar venous pressure is approximately equal to the sum of the vertical distance between the point of puncture and the pressure in the right auricle.

Unfortunately, the pressure in the internal jugular vein cannot be used to calculate the venous pressure below the heart in the living organism. The heart acts not only as a pump on the arterial side but as an outlet on the venous side and therefore breaks the continuity of the venous column. With the blood at rest the column is functionally continuous. During life, with the flow proceeding, the venous pressures above and below the heart are dependent on the heart and also on the resistance and head of pressure in their respective circuits, and are therefore not directly related to each other. This has been demonstrated in an apparatus constructed by one of us (von Storch). Therefore, the lumbar venous pressure cannot be computed from observations on pressure in the internal jugular vein.[6]

Eyster [9] and others have shown that pressure in the right auricle in man varies from 0 to 100 mm. of water. Under conditions of adequate cardiac compensation, this pressure remains the same with the subject in the erect position. The average distance from the right auricle to the level of the lumbar puncture needle was found to be about 350 mm. The sum of this distance (350 mm.) plus the pressure in the right auricle (from 0 to 100 mm.) gives the average range of lumbar cerebrospinal fluid pressure (from 350 to 450 mm. of water). This approximation is confirmatory of the preceding conclusions. The lumbocisternal distance happens also to approximate this sum and probably explains the close correlation of the lumbocisternal distance and the lumbar cerebrospinal fluid pressure in the erect position. Clinical observations have suggested [8] that patients with high systemic venous pressures have also high cerebrospinal fluid pressures when in the erect position. Further observations, however, are needed to confirm this.

SUMMARY

It has been demonstrated that the outer envelop of the craniovertebral system of man is semirigid. The volumetric alterations within this system are minute on change from the recumbent to the erect posture, even when a displacement manometer is used. The normal lumbar cerebrospinal fluid pressure measured with the subject sitting erect bears no simple relationship to the pressure measured with the subject recumbent. The lumbar cerebrospinal fluid pressure in the sitting position is approximately equivalent to the vertical distance between the cisterna magna and the point of puncture. Accurate measurement of this pressure may be obtained only by direct observation. Engorgement of the intracranial veins in man, with consequent increased intracranial venous and cerebrospinal fluid pressures, does not alter the total elastic

9. Eyster, J. A. E.: The Clinical Aspects of Venous Pressure, New York, The Macmillan Company, 1929.

response of the craniovertebral system on assumption of the erect posture. Engorgement of the lumbar intradural veins in man does not alter the normal lumbar cerebrospinal fluid pressure in the erect position. Collapse or distention of the vertebral dura of man plays no more than a secondary rôle in the production of the lumbar cerebrospinal fluid pressure in the erect position. In the presence of a complete subarachnoid block in the upper thoracic region the lumbar cerebrospinal fluid pressure in the erect position is quantitatively normal.

CONCLUSION

The lumbar cerebrospinal fluid pressure in man when in the erect sitting position is a reflection of the intradural venous pressure existing at the point of measurement.

The physicians of the National Hospital permitted these observations to be made on the patients under their care, and Dr. J. C. Greenfield gave many helpful criticisms.

HYPERTENSIVE APOPLEXY AND ITS CAUSATION

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There are few chapters of wider interest in pathology than that of hypertension in its relation to cardiovascular-renal lesions, and particularly to hemorrhage of the brain. Traube[1] (1856) first submitted important experimental evidence to show that increased blood pressure is a consequence of arteriosclerosis, and this was generally accepted till the end of the last century, when more accurate methods of recording the blood pressure were devised. These methods led to renewed interest in hypertension and its associated anatomic lesions. Subsequently, there appeared occasional records of cases of elevated blood pressure in which there was observed no demonstrable arteriosclerosis and no lesion of the kidneys or brain at autopsy. The results of investigation centered in two schools during the early part of this century. One expressed the belief that hypertension is secondary to local or general vascular disease; the other assumed that it is primary and independent of regressive arterial changes. Current conception holds that it may be separated from arteriosclerosis, nephritis and hemorrhage of the brain, but that these are commonly associated lesions. Furthermore, vascular changes incident to hypertension may involve almost any tissue or organ.

By hypertension is meant simply increased tension on the wall of the vessel. It has become so common in recent years that it is frequently loosely referred to as "blood pressure disease." On the contrary, Lange[2] pointed out that hypertension is not an entity but a symptom which is accepted as the "central concept" of a disease. Until more is known about the etiology of these functional disturbances and the reasons for the selectiveness of accompanying anatomic changes in certain tissues and organs, even the so-called pure, or essential, hypertension remains an uncertain entity. The etiologic part of the problem will be left aside in this study. My purpose is to contribute

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From the Pathological Institute, the McGill University Faculty of Medicine; Prof. Horst Oertel, Director.

1. Traube, L.: Ueber den Zusammenhang von Herz und Nierenkrankheiten, Berlin, A. Hirschwald, 1856; Ges. Beitr. z. Path. u. Physiol. **2**:290, 1871; quoted by Lange.[13]

2. Lange, F., in Cowdry, E. V.: Arteriosclerosis: A Survey of the Problem, New York, The Macmillan Company, 1933, p. 501.

something to the second, or anatomic, side in describing and analyzing the intracranial vascular changes, with an effort to trace the causal sequence of these structural changes.

ANALYSIS OF CASES OF ESSENTIAL HYPERTENSION

The pathologic arterial changes in uncomplicated hypertension are distinct from those of arteriosclerosis, although the latter are frequently associated with a slight or moderate degree of clinical hypertension. In this analysis there was therefore a small group of cases in which it was impossible to be sure, clinically or anatomically, whether hypertension or arteriosclerosis was primary. This doubtful group was not included. The term "hypertensive apoplexy" is restricted to conditions which were not associated with the regressive vascular changes of typical arteriosclerosis.

There were only eighteen cases of pure, or uncomplicated, hypertension in the series of one hundred and eight cases of hemorrhage of the brain. Dependent on the duration of disease and the anatomic picture, these were divided into two groups: (1) fifteen cases of hypertension for at least two years in which there was more or less diffuse thickening of muscular arteries and (2) three cases of transient hypertension for a few weeks or months which was not associated with any arterial thickening.

LONG-CONTINUED ESSENTIAL HYPERTENSION

A. General Clinical and Anatomic Analysis.—Analysis of the clinical course in the fifteen cases of hemorrhage of the brain indicates that the high blood pressure became stabilized for several months or years, so that the patient was relatively free from symptoms. There were, however, transient attacks of dizziness and vertigo, and sometimes aphasia or complete loss of consciousness and other signs of intracranial irritation. The heart was always enlarged. With the apoplexy there supervened one or more of three groups of symptoms: those arising from (1) circulatory insufficiency, (2) chronic nephritis and (3) diffuse petechial hemorrhages.

1. Circulatory insufficiency was indicated by more or less acute venous congestion of the lungs and liver, with progressive edema of the extremities. There were sometimes several attacks before the final exit. In all seven cases of massive hemorrhage of the brain there was no marked evidence of circulatory insufficiency before apoplexy occurred. In other words, the hemorrhage in the brain preceded the cardiac collapse.

2. Symptoms of chronic nephritis were noted in only five of the fifteen cases, but there was pathologic evidence of early genuine productive nephritis in an additional seven instances. In all but three of this small series, therefore, there was chronic disease of the kidneys. In four of the five cases of clinical nephritis the condition was diagnosed as chronic interstitial nephritis, and in one case as

chronic parenchymatous nephritis. The anatomic picture of genuine productive nephritis (primary contracted kidney) was definite in all twelve cases. In the cases in which there was a clinical picture of nephritis the kidneys were more contracted and smaller than in the other cases. These observations, moreover, suggest (*a*) that early genuine productive (or interstitial) nephritis may produce no clinical signs or symptoms and (*b*) that whereas clinical evidence of nephritis may not always be present in essential hypertension with apoplexy, medial hypertrophy of small renal arteries is much more frequent than the clinical picture indicates.

3. The distribution of petechial hemorrhages throughout the body was varied. The gastro-intestinal tract was most frequently involved. There were infarctions of blood from engorged terminal segments in the mucosa and submucosa. Next in order were the retina and conjunctiva. Many of the petechiae described here during life were not seen at autopsy, suggesting dissolution and recurrence of extravasated blood cells. Petechiae were observed quite often in the myocardium or endocardium, and in none of the cases was the brain exclusively involved. It is noteworthy that when massive hemorrhages were observed in the brain, there was usually a history of slight exertion an hour or two before, but not at the time of sudden collapse. This may be in some way related to a sustained high arterial pressure.

B. Anatomic Intracranial Vascular Changes.—Gross Description: The most obvious and constant vascular lesion was thickening of the intracranial muscular arteries (fig. 1 *A*). This was generalized (instead of segmentary, as in arteriosclerosis) but varied considerably with the caliber of the vessel. Usually the exposed large arteries at the base of the brain were more thickened than the smaller vessels in the brain substance. The degree of thickening was also variable, but neither of these factors seemed to have any definite relation to the duration or degree of hypertension. A less obvious change was dilatation of the lumen. This varied greatly in different arterial segments and in different cases. In some places it could be seen grossly, while in other districts it could be appreciated only in histologic sections. To summarize, therefore: The arteries resemble somewhat the cordlike thickening of syphilitic endarteritis, but this thickening is more uniform and regular; thus, the arteries appear larger and on transverse section show wide lumens. They differ from the picture of arteriosclerosis by the absence of tortuosity and patchy regressive changes.

The hemorrhages showed great variation in size, number, position and age. Analysis of size is necessarily only relative. In seven instances the blood clot was over 2 cm. in diameter. These massive hemorrhages consist of multiple centers of laminated fibrin and blood cells (fig. 2 *A*). Dissection of the unfixed clot discloses many fine, stiff, threadlike vessels. The suggestion may be raised either that the clot is the result of fusion of small independent foci or that the effect of local pressure produces a spreading field of prestasis about a primary small focus, so that secondary diapedetic hemorrhages occur rapidly in the surroundings. Such massive hemorrhages are probably more frequent in essential hypertension than in arteriosclerosis, and in the latter disease the clot is usually a single laminated mass with a homogeneous center and, on gross dissection, contains few or no small vessels.

The multiplicity of the minute hemorrhages in essential hypertension is an important anatomic feature. In contrast to the massive hemorrhages, which are often solitary, these punctate bleedings are multiple and are usually associated with diffuse hyperemia. Many perivascular foci are so small that they can be seen only on microscopic examination; so one may assume that many are missed

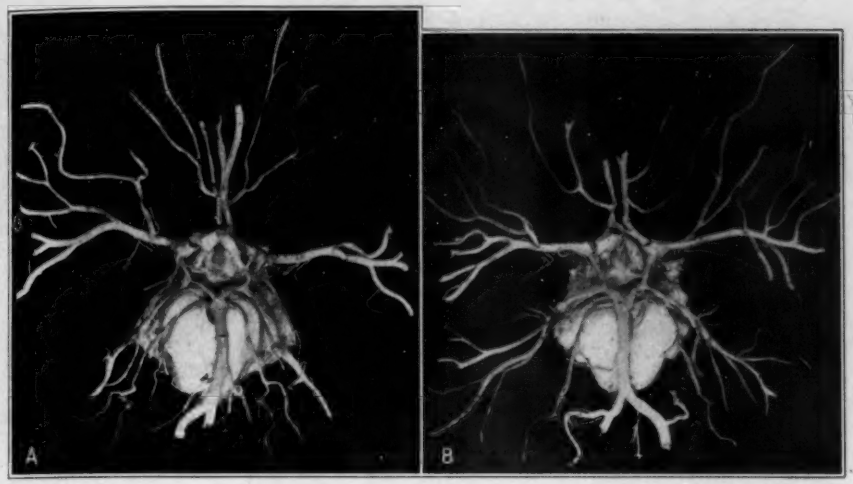

Fig. 1.—Photographs showing dissection of the arteries at base of the brain (*A*) in a case of long-continued essential hypertension, in which there was uniform, cordlike thickening of the arteries, and (*B*) in a case of eclampsia with marked transient hypertension, in which the arteries were well preserved.

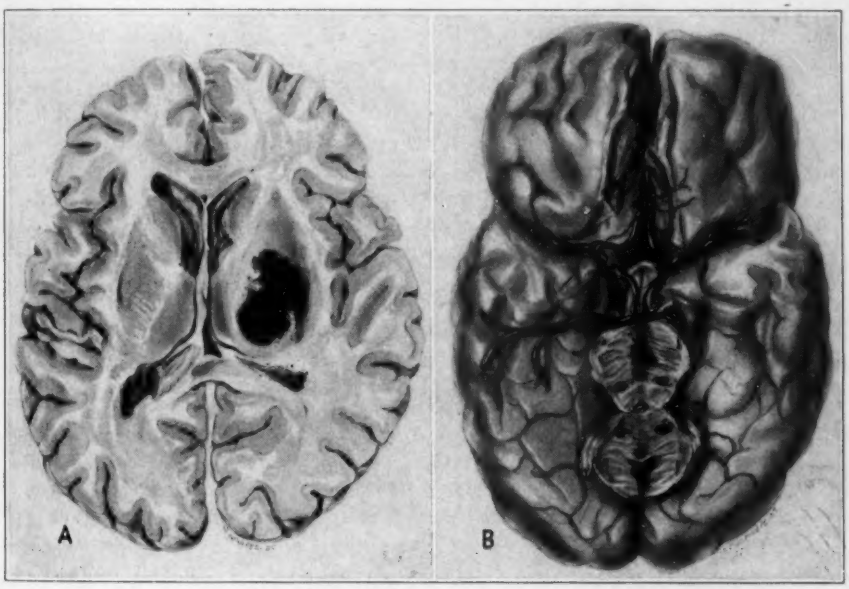

Fig. 2.—(*A*) Massive hemorrhages involving the left thalamus, the internal capsule and the lenticular nucleus, with confluence of multiple concentrically laminated masses of blood, and (*B*) symmetrical focal hemorrhages in the pons, with uniform, cordlike thickening of the exposed arteries.

in areas which are not examined. They apparently may occur anywhere, but on gross examination in this small series the sites were in the following order of frequency: the corpus striatum, the optic thalamus and the pons.

Extravasated blood in the brain appears to undergo the same changes in color that occur in other tissues. Its appearance depends on the quantity of blood and on its duration outside the vessel. All shades of color in such clots are therefore seen in different areas of the same specimen. This indicates repeated insults, extending over months or even years. Furthermore, one is frequently able to pull off a thin layer of blood pigment and organizing tissue from about small muscular arteries, carrying the adventitia with it but leaving the two inner coats intact. This evidence (confirmed by microscopic sections) points to the fact that the blood does not come from the lumen of these muscular arteries. Such perivascular clots appear as enveloping mantles and as round, small, nodular projections. Pick [3] described them as large as a cherry, but that is much larger than any I have encountered. Some were, no doubt, included in the classic description of syphilitic miliary aneurysm of Charcot and Bouchard [4] many years ago, and on account of their close resemblance to this lesion, Schwartz [5] referred to them as pseudo-aneurysms. The term is appropriate, as superficially they resemble true aneurysm, while dissection with a hand lens shows a smooth, intact intima and media.

I have not observed thrombosis of the large arteries and veins to be as frequent in true hypertensive apoplexy as in the arteriosclerotic type. Capillary thrombi, on the other hand, are numerous. It is impossible to distinguish arterioles from venules with certainty, but I have seen thrombi in small veins nearly as frequently as in small arteries. One is inclined to believe, as indicated by Cobb and Hubbard,[6] that in autopsies performed as a routine more attention is often given to intracranial arteries than to veins; hence, thrombi in these veins may be frequently overlooked.

Microscopic Technic and Description: The study of terminal vascular segments was made mostly from large frozen sections, using a modified Christeller [7] technic. This was found to have several advantages: 1. There is no shrinkage due to drying except at the marginal cortex, because the sections are not dehydrated. 2. The thickness and large size of the sections permit the study of unusual lengths of small vessels and serve more readily to identify topographic districts. 3. Delafield's hematoxylin stains nuclei brown, while trinitrophenol and acid fuchsin accentuate the walls of vessels and red blood cells. The disadvantages are that the leptomeninges, the marginal cortex and the large arteries are often hopelessly torn and distorted, in spite of careful manipulation.

In these topographic frozen sections leukocytes and red cells were extremely numerous in very small foci about many terminal districts. They were usually situated at the acute angle of branching or on the convex side of a bend in a capillary loop (figs. 3 *A* and 4 *C*). When the endothelial wall could be defined, it

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3. Pick, L.: Ueber die sogenannten miliaren Aneurysmen der Hirngefässe, Berl. klin. Wchnschr. **47**:325, 1910.

4. Charcot, J. M., and Bouchard, C.: Nouvelles recherches sur la pathogénie de l'hémorragie cérébrale, Arch. de physiol. norm. et path. **1**:110, 1868.

5. Schwartz, P.: Die Arten der Schlaganfälle des Gehirns und ihre Entstehung, Berlin, Julius Springer, 1930.

6. Cobb, S., and Hubbard, J. P.: Cerebral Haemorrhage from Venous and Capillary Stasis, Am. J. M. Sc. **178**:693, 1929.

7. Christeller, E.: Atlas der Histotopographie gesunder und erkrankter Organe, Leipzig, Georg Thieme, 1927.

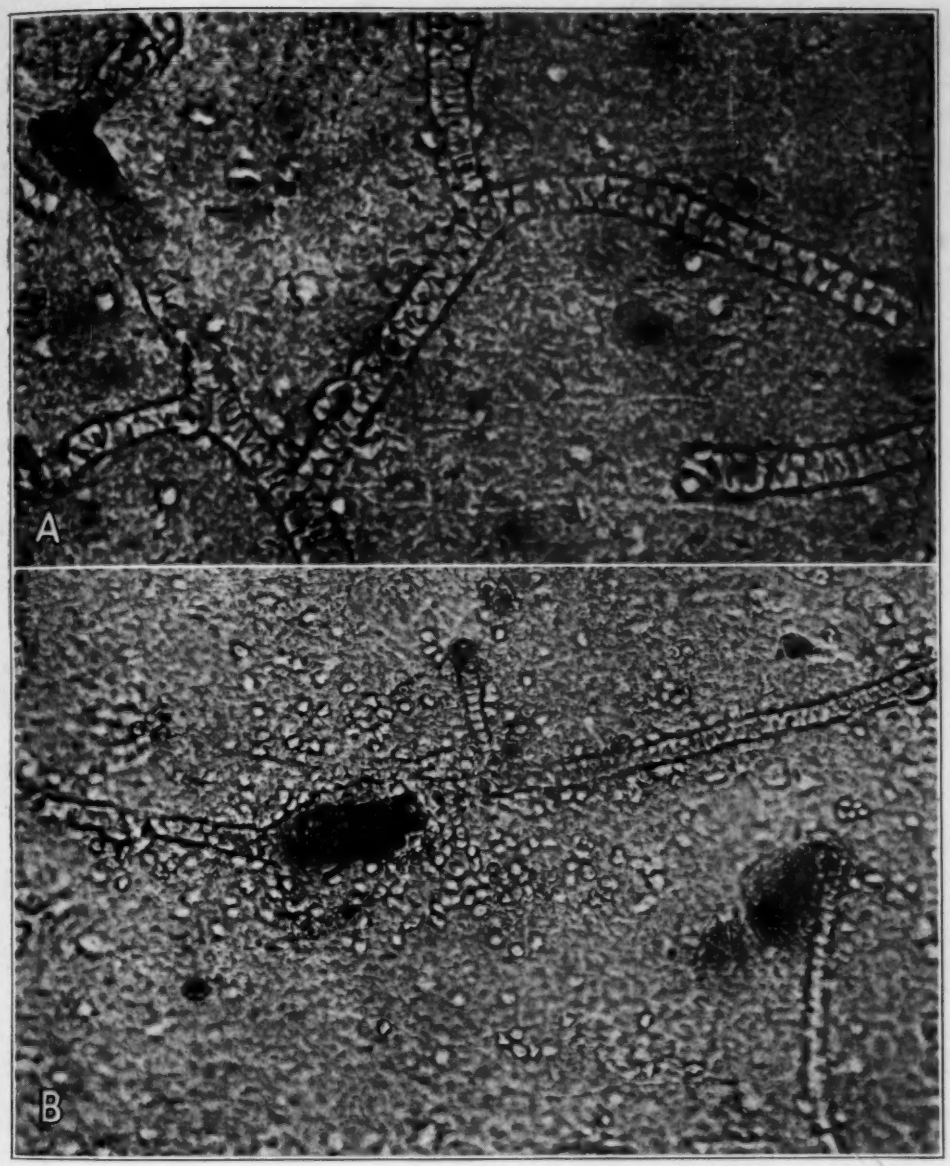

Fig. 3.—Photomicrographs: *A* is a capillary district in the midbrain in a case of prolonged (essential) hypertension, showing scattered, extravasated red cells, mostly at the angle of branching. The blood cells are conglutinated rather than agglutinated. × 240. *B* shows the punctate extravasation of blood cells extending from a terminal segment in the brain in a case of transient hypertension. The blood cells in the vessel at either end of the hemorrhage are conglutinated. This indicates that blood movement continued after the hemorrhage occurred. × 200.

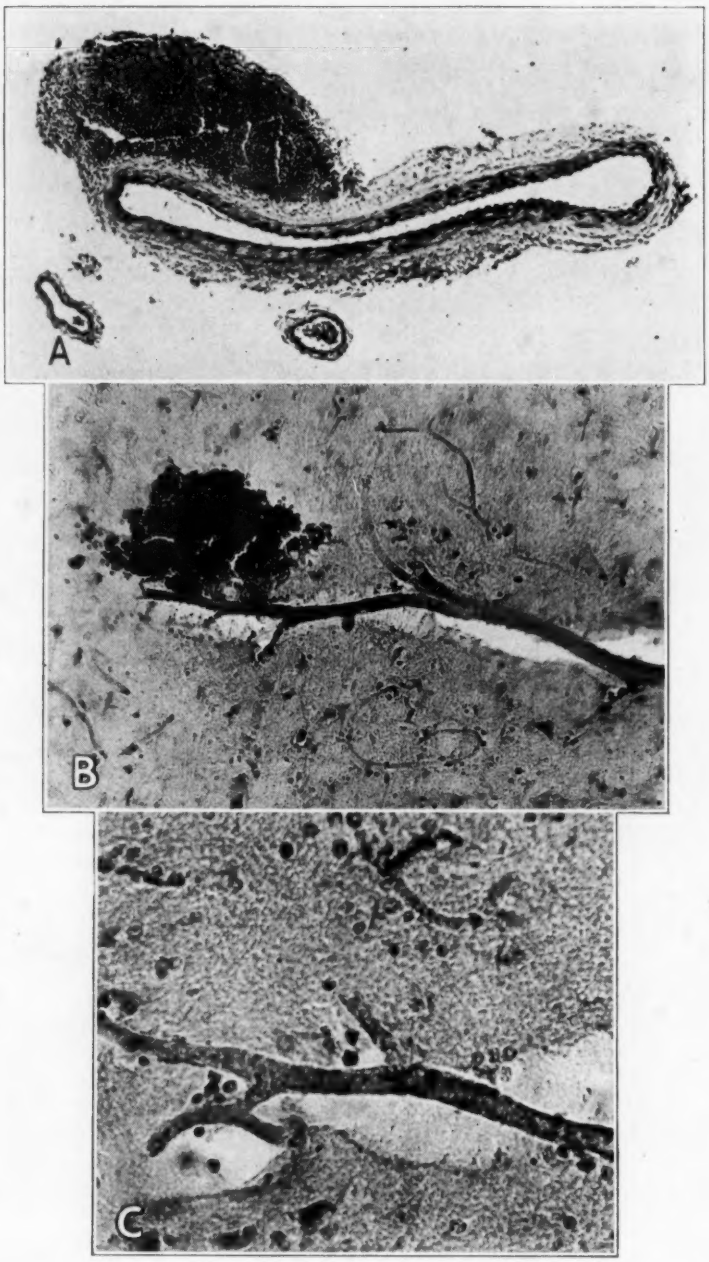

Fig. 4.—(*A*) Focal adventitial hemorrhage from the vasa vasorum of a muscular artery dissected from the brain in a case of prolonged hypertension. The inner coats are intact, and the media is slightly uniformly thickened. × 75. (*B*) Focal hemorrhage, probably from terminal districts adjacent to the intact small artery, in a case of prolonged hypertension. The distal half of this vessel is thrombosed, while the cells in the proximal half are still conglutinated. × 90. (*C*) Scattered blood cells at the acute angle of branching capillaries, in a case of eclampsia with marked transient hypertension. × 180.

was always intact. Sometimes there was only a small cluster of blood cells, while in other fields there were small fused masses of blood constituents beside, or encircling, the vessel (figs. 3*B* and 4*B*). There was sometimes a narrow zone of fused, disintegrating brain tissue between the vessel and the hemorrhage; but there is no reason to assume (as Rosenblatt did) that this occurred before the bleeding, for it was absent when there were few perivascular blood cells.[8] It appears that this disintegrating zone is the result of vascular functional disturbances and is coextensive with the amount of the hemorrhage. This occurs, of course, before stasis and thrombosis are complete (prestatic blood flow). It is, therefore, not initiated by the thrombosis, which is the result of the final localized circulatory collapse.

Thus also, the frequency of thromboses in these terminal segments was variable. 1. When the bleedings were small, the cells within the engorged capillaries were usually conglutinated with well defined outlines. There was often evidence of separation of serum from the red and white cells (as occurs during peristasis in experiments on blood flow in the rabbit's mesentery), but these districts were not thrombosed. 2. When the bleedings were large, terminal thrombi were more frequent but were not necessarily present. The outline of blood cells was lost, and the dilated terminal districts were filled with an agglutinated fused mass of cells and serum (compare figures 3*A* and *B* and 4*B*). 3. There were occasionally seen localized districts of collapsed terminal segments without perivascular hemorrhage in which the surrounding brain tissue showed evidence of necrosis. In some of these regions there was a thrombus in the proximal artery or vein. The functional explanation for this anatomic picture will be discussed presently. For this purpose, comparison with certain other experimental observations is in order.

Direct examination of the living rabbit's mesentery shows that any kind of vascular irritant of definite intensity and duration will lead to hemorrhages by diapedesis from capillaries and venules, but never from the arterial side. Histologic examination suggests that many of the bleedings into the brain substance in hypertension arise also from terminal vascular districts. However, the source of the blood which appears even grossly about many of the small muscular arteries must be explained further. Microscopic study of these arteries indicates two possible sources: 1. Some are retrograde collar extensions from larger bleedings in terminal districts. These form narrow perivascular foci in the softened brain about larger masses of blood clot (fig. 5). 2. Some arise from the vasa vasorum of the well preserved muscular arteries. This is indicated by their intense hyperemia and the limitation of the extravasated blood to the stretched outer (adventitial) membrane. The blood in these instances appears to be coextensive with the vascular wall and not primarily perivascular (fig. 4*A*). For this reason, the clot and adventitial coat may be stripped from these arteries, as already noted, leaving an intact, well preserved media and intima.

TRANSIENT HYPERTENSION

The three cases of this type were in pregnant women, all of whom had a history of repeated eclamptic convulsions and a definitely high blood pressure. It is perhaps noteworthy that in two other cases of

8. Rosenblatt attempted to bring such necroses of the brain into relation with a ferment action.

death from eclampsia, in which there were fewer, milder convulsions, no gross or microscopic hemorrhages were shown in the brain. The average age of these three patients was 34 years, as compared with that of 41 years in the fifteen cases of prolonged essential hypertension.

Intracranial Vascular Changes.—Gross Description: In no instance was there evidence of thickening of any arteries at the base of the brain or of small muscular arteries on its cut surface (compare fig. 4 *A* and *B*). This constitutes the

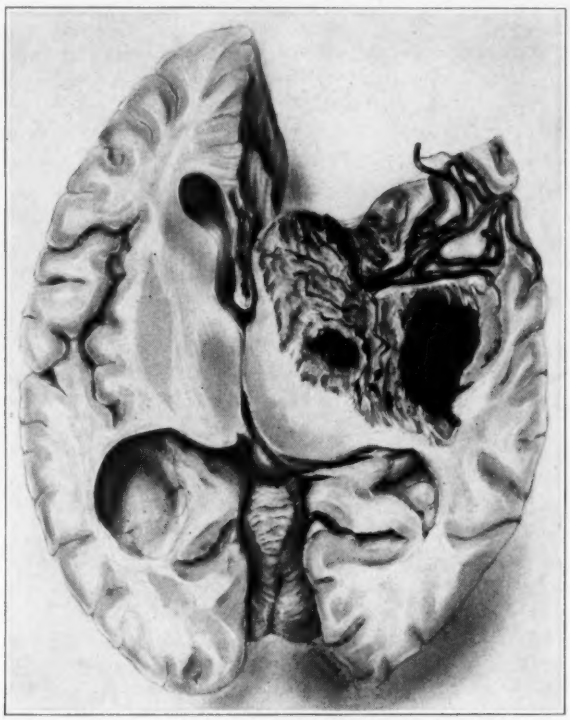

Fig. 5.—Drawing showing dissection of small arteries to the right basal ganglia. Note the perivascular collars and punctate distribution in the softened brain near two massive hemorrhages. There are also small punctate hemorrhages in ependymal vessels.

most obvious difference between this group and the group with prolonged hypertension.

There were no massive hemorrhages, although in one case were two foci, nearly 1 cm. in diameter, situated in the left side of the midbrain. In the other two cases there was diffuse intense engorgement of vessels throughout all parts of the brain but no definite gross hemorrhage. No pseudo-aneuryms were observed in the small muscular arteries nor pigmented foci of organizing blood.

Microscopic Description: The absence of hemorrhages from the vasa vasorum into the adventitia of small muscular arteries was confirmed. Extravasations were entirely from terminal vascular districts, as illustrated in figure 4 *C*.

COMMENT

Cases of essential hypertension form a heterogeneous group, for the objective symptoms are few and inconstant. Apart from the high blood pressure and the muscular hypertrophy of the heart and arteries, the clinician is forced to rely largely on subjective complaints of a functional character. This has led to the adoption of numerous tests for estimating the vascular function in hypertension. Lange has shown, for example, that "the reaction of the blood vessels of the arm to heat and cold is more pronounced in hypertonia than under normal conditions." That is, the normal physiologic response to the irritant is substituted by a more extreme and prolonged alteration in arterial pressure. Furthermore, Kaufmann,[9] Hanse,[10] Westphal[11] and others have shown that in hypertension marked changes in pressure may result from a slight irritation and that physical irritants which in the control animal produce only a transient rise in blood pressure cause a much greater, and often fatal, rise in cases of hypertension. It is therefore established that arteries in hypertension have a more ready vascular response to stimulation than do normal arteries. In other words, there is hyperirritability with increased neurovascular tonus.

From the foregoing description of the intracranial vessels in cases of hypertension, it is obvious that one is concerned primarily with two anatomic conditions and changes: (1) arterial thickening and (2) hemorrhage. Since one must recognize an increased neurovascular tonus in essential hypertension, what relation, if any, has this functional alteration in these two pathologic lesions?

The arterial thickening is due almost entirely to the increased diameter of the muscular media. This coat maintains tonus during vascular contraction, while the collagen elastic fibers take over that function during dilatation. The hypertrophy of the muscular media is apparently compensatory to long-continued increased vascular tonus. It is analogous to, and often associated with, similar changes in the myocardium. This compensatory muscular hypertrophy is absent in transient hypertension, probably because the time is too short for its development. The difference in degree of muscular hypertrophy in arteries of different caliber may be assumed to depend at least partly on variations in the degree and duration of the functional irritant. In

9. Kaufmann, F.: Pathologie des arteriellen Blutdrucks, in Bethe, A.; von Bergmann, G., and others: Handbuch der normalen und pathologischen Physiologie, Berlin, Julius Springer, 1927.

10. Hanse, A.: Zur Klinik der Apoplexie, Deutsche med. Wchnschr. **51**:938, 1925.

11. Westphal, K.: Untersuchungen zur Frage der Entstehungsbedingungen des genuinen arteriellen Hochdrucks, Ztschr. f. klin. Med. **101**:545, 1924-1925.

this connection Ricker's [12] causal theory for proliferative and regressive arterial changes is noteworthy and well supported by experimental experience (Lange [13]). These changes in the blood vessels under the action of irritants may here be briefly summarized: A weak or mild irritant produces vasoconstriction and an increased nutritional exchange over the normal in the arterial coats from both the intimal and the adventitial side. The blood pressure is carried by the media; the intima is relaxed, without its fibers being loosened. Over a long period this functional change produces compensatory hypertrophy of the muscular media. A somewhat stronger, but still moderate, irritant lowers constrictor irritability and is therefore followed by dilatation of a muscular artery (blood peristasis in the arterial wall). Loosening and edema of the coats are here more marked; the medial coat is relaxed, and the blood pressure is carried by the stretched fibro-elastic intima (intimal hyperplasia). Intimal proliferation predominates here over medial hypertrophy. A strong irritant, finally, produces blood stasis in a much dilated and stretched arterial wall (muscular paralysis), which in turn undergoes regressive changes, so that necrosis and calcification follow. Moderately strong irritants lead therefore to the morphologic picture of advancing arteriosclerosis, while the mild irritants (with which I am concerned here) produce a picture of muscular hypertrophy. This therefore represents the anatomic equivalent of hypertrophy (Dietrich [14]).

Ricker's fundamental concepts of the importance of the influence of nerve impulses on the control of the size of blood vessels offer a plausible sequence of events for the vascular lesions but do not account for the factors which may be responsible for the stimulation of these vasomotor nerves. There is evidence that nerve stimulation is not always essential to changes in the caliber of vessels. Thus, Ehrich and Cohn have demonstrated the complete absence of nerves in the vessels of the yolk membrane of the chick embryo, and with them Lange [15] showed that "the vascular reactions in this region are governed by the same laws which Ricker has demonstrated for blood vessels that are supplied with nerves." In the fully developed organism, however,

12. Ricker, G.: Sklerose und Hypertonie der innervierten Arterien, Berlin, Julius Springer, 1927.

13. Lange, F.: Studien zur Pathologie der Arterien, insbesondere zur Lehre von der Arteriosklerose, Virchows Arch. f. path. Anat. **248**:463, 1924.

14. Dietrich, K.: Wege zur Pathologie der Arterien mit Berücksichtigung ihres Verhaltens bei Hypertonie, Verhandl. d. deutsch. path. Gesellsch. **24**:308, 1929.

15. Lange, F.; Ehrich, W., and Cohn, A. E.: Studies on Blood Vessels in Membranes of Chick Embryos: Absence of Nerves in the Vascular Membrane, J. Exper. Med. **52**:65, 1930.

there seems little if any doubt that nerve stimulation is of paramount importance in alterations in the caliber of all vessels in man. Thus also, the important psychic circulatory effects are brought about by nerve carriage. This does not, however, exclude the possibility that there may also be subordinated humoral (?) influences acting directly on the contractile cells. While there is therefore considerable evidence for assuming that sustained provincial or general constriction of muscular arteries leads to their hypertrophy, its relation to the extravasations of blood still requires to be accounted for.

There is much experimental evidence to indicate that hemorrhages by diapedesis are independent of the kind of irritant (whether mechanical, bacterial or chemical) but depend on its duration and intensity. Diapedesis in the living pancreas and mesentery of rabbits following the application of all sorts of irritants has been repeatedly recorded by me in using the Loeffler and Nordmann [16] modification of Ricker's apparatus.[17] I have also observed such changes after the injection of room air into the aorta.[18] Somewhat similar vascular phenomena have been recorded by Forbes [19] in his study of leptomeningeal vessels in living cats. It is surprising to the observer to note large and rapid hemorrhages in such diapedesis, a fact already emphasized by Cohnheim. These experiments on animals point to a similar mechanism for hypertensive apoplexy. Here also, the arterial segments are under long-continued constrictor irritation, up to and including the terminal vascular districts. Under such circumstances the vessels of these terminal districts (capillaries and arterioles) become fatigued (paretic) after a time; that is, they lose their response to stimuli and dilate, while the proximal muscular arteries remain constricted for a longer time. The resultant slow movement of blood in terminal districts (peristatic hyperemia) leads to increased permeability of their walls, possibly from the incompletely oxygenated blood by which these cells are nourished. Through these vessels passes therefore blood fluid (liquor diapedesis). As blood movement progressively declines (increasing peristatic state and centripetal spread), white cells migrate between the swollen cells of capillaries and venules (leukodiapedesis), and finally there occurs

16. Loeffler, L., and Nordmann, M.: Leberstudien, Virchows Arch. f. path. Anat. **257**:119, 1925.

17. Ricker, G.: Die Methode der direkten Beobachtung der lokalen Kreislaufstörungen und die Verwertung pathologischanatomischer Befunde in den Kreislaufsorganen für die Pathologie derselben, in Abderhalden, E.: Handbuch der biologischen Arbeitsmethoden, Berlin, Urban & Schwarzenberg, 1924, vol. 8, p. 540.

18. Chase, W. H.: Anatomical and Experimental Observations on Air Embolism, Surg., Gynec. & Obst. **59**:569, 1934.

19. Forbes, H. S.: The Cerebral Circulation: Observations and Measurement of the Pial Vessels, Arch. Neurol. & Psychiat. **19**:751 (May) 1928.

diapedesis of red cells. If this paretic dilatation is rapid, however, red cells may appear almost at once. It is noteworthy that there occurs no interruption in blood flow beyond the points of diapedesis; yet an entire low power microscopic field may be covered with blood in as short a time as two minutes. If blood movement ceases (stasis), cell agglutination and thrombosis soon follow and infarction results.

These observations are distinctly opposed to the earlier conception of Westphal, who expressed the opinion that arterial spasm and anemia are the cause of hypertonic hemorrhage of the brain. He stated that spasm of the blood vessels (anemia) produces degeneration of perivascular nerves and thereby weakens the arterial wall and permits diapedesis. But, as is amply demonstrated by experiments, such a vascular spasm in larger arteries is followed not by anemia but by hyperemia (peristasis and prestasis) of terminal vessels. While it is possible that the milder functional derangements may in such cases be explained by arterial spasm with associated slower movement in the terminal districts alone, diapedesis in such districts does not occur without definite (paretic) vasodilatation in these terminal segments, that is, with hyperemia. It is therefore unlikely that spasm itself is the direct cause of bleeding in the brain in hypertension, although it precedes the functional changes which permit diapedesis in the production of peristatic and prestatic hyperemia. This explanation was also assumed by Scriver and Oertel [20] for bilateral renal necrosis in pregnancy.

Finally, one comes to an account of the curious, purely adventitious, hemorrhages of muscular arteries. If it is accepted (as the abundant experimental evidence here briefly outlined indicates) that pronounced, long-continued hypertension leads to paresis and paralysis, primarily in terminal districts (capillaries and arterioles), it is perhaps reasonable to assume that the proximal arteries may, under sustained stimulation, also become muscularly fatigued and paretic. Indeed, Ricker's original observations on circulatory changes under stimulation supported this contention as well as the recent observations by Koeppen [21] on electric vasomotor death. The dilatation of these arteries reflects on the already retarded blood movement in their vasa vasorum, and a strong peristatic flow and hemorrhage take place from them into the adventitial sheath. If this assumption is correct (to which, indeed, some of my anatomic observations point), the hypertensive arterial functional disturbances resolve themselves into a proximally traveling, more or less rapid vascular fatigue (paresis), which, commencing in

20. Scriver, W. de M., and Oertel, H.: Necrotic Sequestration of the Kidneys in Pregnancy, J. Path. & Bact. **33**:1071, 1930.

21. Koeppen, S.: Elektrizitätsschäden im Tierexperiment mit besonderer Berücksichtigung des elektrischen Todes, Virchows Arch. f. path. Anat. **290**: 460, 1933.

the terminal districts, overtakes in time even muscular arteries. Its effect on the blood movement becomes manifest by a peristatic and a prestatic blood flow, during which various amounts of blood escape into the surrounding districts (infarctions). It is ended by stasis with thrombosis.

Finally, a word in regard to symmetrical apoplexies, which are not infrequent in primary hypertension: They are usually seen in the pons (fig. 2*B*). In the absence of a mechanical block in the vessel in the midline leading to or from bilateral districts, some other explanation must be sought. Schwartz [5] assumed repeated hypertonic pressure waves which are carried along a large artery or vein in a different direction from that in its terminal districts. These high pressure waves may produce functional circulatory derangement resulting in traumatic insults, which are manifested by various degrees of hemorrhage and infarction, depending on the intensity of the irritant. The arteries supplying the pons, for example, are mostly branches of the common basilar artery. Injections show that these small branches run peculiarly at right angles, in a vertical and transverse manner. This distribution of hemorrhages is probably influenced by pressure effects in symmetrical territorial districts, as well as by hypertonic pressure waves carried along bilateral branches of a common vessel in the midline.

SUMMARY

A clinical and anatomic analysis is recorded of eighteen cases of hypertension and hemorrhage of the brain in which there was no arteriosclerosis.

Hypertension is characterized functionally by a condition of vascular hyperirritability and increased neurovascular tonus. Its anatomic equivalent is hypertrophy of muscular arteries and hemorrhage.

In long-continued essential hypertension, even large hemorrhages may occur in the brain by diapedesis from terminal districts and from the vasa vasorum of hypertrophied paretic muscular arteries.

In transient hypertension, hemorrhages in the brain from the vasa vasorum and hypertrophy of muscular arteries are absent, while petechial hemorrhages from terminal districts are not infrequent.

The histologic picture of small vessels in large topographic frozen sections of the brain is similar to that of small vessels in the living rabbit's mesentery after the application of any form of irritant. The neurovascular mechanism for these hemorrhages has been briefly described.

Symmetrical bilateral hemorrhages of the brain in hypertension are readily explained by the neurovascular theory of causation.

FACIAL TIC IN RELATION TO INJURY OF THE FACIAL NERVE

AN EXPERIMENTAL STUDY

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Kuhne's much cited demonstration of bifurcating axons to the gracilis muscle of the frog has not been successfully repeated in mammals. In fact, it remains to be shown that a single axon can normally supply fibers to two distinct muscles or to spatially separate portions of the same muscle. On the other hand, there is abundant evidence that under pathologic conditions one axis-cylinder may arborize over a wide area. Langley and Anderson [1] and, almost contemporaneously, Kilvington [2] demonstrated the branching of axons by mechanical and electrical stimulation of motor nerves regenerated after being severed and reanastomosed in various combinations. The histologic studies of Ramón y Cajal [3] also exhibited regenerating axons greatly distorted and frequently branching in the neighborhood of the injury. However, these physiologic and anatomic observations have never been correlated in a single experiment in which both the axon reflex and its morphologic raison d'être, the branched axon, were shown to be present.

The present communication relates to the condition of the facial nerve after functional recovery from injury sufficient to bring about paralysis of the facial musculature.

MATERIAL AND RESULTS

The material consisted of a series of twenty-seven rhesus monkeys (Macaca mulatta) in which the facial nerve of one side was injured just distal to the stylo-

This study was aided by a grant from the Carnegie Corporation.

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1. Langley, J. N., and Anderson, H. K.: The Union of Different Kinds of Nerve Fibers, J. Physiol. **31**:365-391, 1904.

2. Kilvington, B.: An Investigation on the Regeneration of Nerves, Brit. M. J. **1**:935-940, 1905.

3. Ramón y Cajal, S.: Degeneration and Regeneration of the Nervous System, London, Oxford University Press, 1928.

mastoid foramen (1) by complete section and resuture with or without insertion of a nerve graft (fifteen animals), (2) by partial section (four animals), (3) by freezing (three animals) or (4) by injection of alcohol (five animals). After an interval averaging forty-four days, movement was again observed in the paralyzed muscles. Soon after the first evidence of returning function there also appeared purposeless twitching movements which involved various muscle groups, and at times the entire area which had previously been paralyzed. These ticlike movements previously described by one of us (A. B. D.[4]) became apparent in from fifty-two to seventy-nine days after operation. For several months, as the paralysis regressed, the spasmodic movements spread over a wider area, but when recovery ceased their progression was also arrested. When fully developed they usually involved large parts or the entirety of the facial musculature, but in a few animals only a single muscle, such as the levator labii superioris or the helicinus muscle, was affected. In general the gravity of the tic was proportional to the degree of disturbance in the bed of the facial nerve rather than to the amount of paralysis. Thus, the severest tics were seen after section of the nerve, whereas tics developing after freezing or injection of alcohol were less severe, even though these procedures had also resulted in complete facial paralysis. All the animals were kept at least three months, while twenty-four lived a year and eleven survived into the third year. In no case was the slightest abatement of the tic noted.

When these adventitious facial contractions were analyzed, it became apparent that they were synchronized with a purposeful movement which was taking place in some portion of the facial musculature. Thus, while many of the tics involved the platysma, the orbicularis oris or the auricular musculature, they were nevertheless precipitated at the same moment as closure of the eyelids. This type of so-called blink tic was present in all cases of nerve section and injection into the nerve, as well as in two cases in which the nerve was frozen, and was the most conspicuous sequel of injury to the nerve. Four animals showed purposeless rhythmic movements of the platysma muscle or the musculature of the eyelid, cheek or ear which were synchronous with respiration. All the tics were more apparent during strong facial movements, and these "respiratory tics" were greatly accentuated during hyperpnea, when the nares were vigorously dilated. Several animals showed more sustained unilateral contraction of the frontalis muscle or the cervical platysma muscle when the cheek pouch on the affected side was being emptied, while two closed the eye on that side in a curious irregular flutter during this performance. Two other animals were forced to close the lid on the affected side during the facial movements incidental to chewing.

The following groups of experiments were designed to elucidate the relationship between the tics and orderly action in the facial musculature. In six animals showing a marked blink tic, the electrically excitable

4. Duel, A. B.: History and Development of the Surgical Treatment of Facial Palsy, Surg., Gynec. & Obst. **56**:382-390, 1933.

cortex was laid bare on both sides, the animals being under light ether anesthesia. Stimulation of the frontal and parietal lobes was carried out by means of a 60 cycle current of from 0.5 to 2 milliamperes. From the cortex opposite the side of injury to the nerve it was possible to obtain many normal facial movements, such as pursing the lips, licking, chewing, retraction of the ears and wrinkling the brow. In these movements there was no suggestion of the tic, but stimulation of any point which produced closure of the lids brought forth the adventitious movement. Furthermore, it was possible to provoke this from the ipsilateral cortex in the bilaterally operating upper facial fields. Thresholds for these cortically excited performances were equal on the two sides, both in voltage and in the amperage required—a phenomenon which excluded any factor of central hyperexcitability from the mechanism of the mass contractions.

Although the tic could be elicited by stimulation of the cortex, it nevertheless persisted in the absence of the cerebral hemispheres. In four animals the entire hemisphere opposite the side of the tic was removed. After the operation both the voluntary and the reflex closure of the lids were still possible and the blink tics persisted. In two other animals voluntary closure of the lids was abolished—in the one case, by bilateral removal of all the cortex anterior to the central sulcus and, in the other, by sherringtonian decerebration. In both these animals the corneal and conjunctival reflexes could still be elicited, and with them the blink tic. Again, with the von Frey needles and hairs as gages of threshold, no difference was found between the two sides to indicate a factor of central hyperexcitability in the tic. This evidence placed the mechanism of the adventitious facial movements low in the motor pathway and pointed to confusion of innervation in the periphery.

Injury and repair of a nerve trunk, such as the facial nerve, give opportunity for peripheral confusion of two sorts: Either nerve fibers, totally misdirected in regeneration, may come to supply muscles with which no original connection existed, or, by branching, one regenerated axis-cylinder may innervate a large portion of the facial field.

The next series of six experiments was concerned with the functional demonstration of axonal branching on the side of the regenerated nerve. A single experiment typical of all will be reported in detail.

The animal selected showed a generalized blink tic involving the brow, mouth and nuchal platysma muscle. With the monkey under ether anesthesia, three large branches of the facial nerve were exposed on each side, and their distribution was determined by unipolar stimulation. On the side of the tic, stimulation of the temporal branch (*AB*, in figure 1) resulted in wrinkling the brow, closure of the eye and elevation of the upper lip. After the nerve had been cut, stimulation of the distal segment, *B*, still gave wrinkling of the brow and closure of the eye, while excitation of the central stump, *A*, gave closure of the eye and elevation of the upper lip. Moreover, these responses were obtained after the

facial nerve had been severed from the central nervous system at its point of exit from the medulla. (In other experiments the nerve was sectioned at the stylomastoid foramen, with similar results.)

Thus was eliminated the possibility of a reflex response to stimulation of sensory fibers in the facial nerve, and the mechanism was shown to operate entirely in the periphery. Here the presence of branched axons offered the only anatomic basis for the phenomenon. Since nerve fibers conduct equally well in both directions, excitation set up at any point in an axon will be propagated throughout its entire extent. Thus, impulses initiated in motor fibers in the central stump, *A*, of the nerve *AB* would be conducted centrally, but at points of branching (presumably the point of injury, *S*) impulses would also pass

Fig. 1.—Diagram of the main branches of the facial nerve. *S* indicates the point of injury to the nerve. *AB*, *CD* and *EF* designate points of the nerve at which electrical stimulation was carried out.

distally in the branch *CD* to elicit muscular contraction in the lip. That the injury does in fact permit such dispersion of the nerve impulses was shown by making progressively more distal sections of the nerve, beginning proximal to the injury. Finally, a point was reached at which response from the central end of any facial branch was abolished. This invariably lay just peripheral to the region of injury.

This demonstration of a phenomenon resembling the normal axon reflex was readily made in other branches of the facial nerve on the side of injury. For example, stimulation of an intact zygomatic branch, *CD*, gave closure of the eye and strong retraction of the whole upper

lip. After this nerve had been cut, stimulation of the distal segment *D*, still yielded the same movements of the eyelid and mouth, but on excitation the central end, *C*, also gave responses of the eye and mouth, e. g., movements in the outer portion of the orbicularis oculi muscle and elevation of the corner of the mouth. Similarly, the intact cervical branch, *EF*, on excitation gave closure of the eye, retraction of both the upper and the lower lip and drawing of the cervical part of the platysma muscle. After the cut, stimulation of the distal segment, *F*, evoked the same movement of the lower lip and the platysma muscle, while from the central end, *E*, were obtained the movements of the lid and upper lip elicited from the intact nerve.

On the normal side the findings were quite different. Here stimulation of the cervical, zygomatic and temporal branches of the facial nerve yielded more or less discrete movements of the lower, middle and upper portions of the face—never a mass contraction of the entire facial field, as on the side of operation. When these branches were cut and the distal ends stimulated, the responses were the same as those obtained from the intact branch. In contrast, stimulation of the central stumps resulted in no movement when the electrodes were applied to the nerve 1 cm. or more from the nearest branch. Stimulation close to branches often resulted in spread of the stimulus to an intact branch, with a resultant muscular contraction over a very limited area contiguous to that branch. This jumping of the stimulating current could readily be distinguished from the mass responses which were obtained from all points on the regenerated nerve.[5]

With physiologic evidence for the presence of branched axons on the side of operation, it remained to demonstrate them anatomically. Three animals, all showing marked tics, were selected. In the first there had been complete section of the facial nerve with the insertion of a graft; in the second the nerve had been "hemisected," while in the third the nerve had been so severely frozen with ethyl chloride that facial paralysis had resulted.

In each case the nerve was dissected from the facial canal, and a specimen was removed containing the site of injury together with portions of the nerve proximal and distal to it. Corresponding specimens were also taken from the normal side. The material, fixed in a 10 per cent solution of neutral formaldehyde, was treated by Bielschowsky's silver impregnation method and sectioned at 15 microns. The regions of injury conformed in general to the descriptions of similar material already detailed by Ramón y Cajal. Figure 2*B* shows a low power view of a region near the nerve graft. The axons varied extremely in size and in the degree of myelinization, but the majority were of medium size. Many fibers were varicose, while the larger ones formed whorls or doubled on themselves. Bifurcating fibers (figure 2*C* and *D*) were common, and numbers

5. Dr. Edmund P. Fowler Jr. assisted in the aforementioned phases of the work.

of axons were seen arborizing into three or four branches. In the normal nerve (figure 2 *A*) the fibers were uniform in size and myelinization. No whorls, skeins or branching axons were seen.

Fig. 2.—(*A*) Normal facial nerve and (*B*) regenerating facial nerve from the region of the nerve graft; Bielschowsky stain, × 420. *C* and *D* show bifurcating fibers from a regenerating facial nerve; × 940.

The physiologic and the anatomic evidence thus agree in demonstrating the presence of branching axons in the regenerated facial nerve, and the physiologic evidence shows further that branches of one axon may be distributed to innervate portions of the facial musculature as far apart as the frontalis and the nuchal platysma muscle. This condition provides an adequate basis for the mass contractions—the so-called facial tics—which follow on injury to and repair of the facial nerve in the experimental animal. However, whether or not this is the entire mechanism of the posttraumatic tic is undetermined, since there remains the possibility that during regeneration nerve fibers which originally supplied one muscle become totally misdirected to supply quite another muscle and yet still act when the original group is brought into play. In the presence of a preponderant number of branching axons, this possibility could neither be verified nor ruled out. Since numerous normal movements of the mouth and ear were obtained from the cortex, it appears that many fibers had established connection with one set of peripheral muscles only, but whether this was their original connection or whether the central nervous system had reeducated itself to employ new connections suitably is not in evidence. Certainly, such reeducation entirely within the facial nucleus must present less difficulty than reeducation when a foreign nerve, such as the hypoglossal, the glossopharyngeal or the auriculotemporal nerve, is used to innervate the facial musculature; yet in such cases (Ballance and Duel [6]) considerable functional readjustment is made. In the present experiments the lack of any suppression or modification of the tic movements, once these had reached a maximum, speaks for the presence of bifurcated axons and against any considerable participation of totally misdirected nerve fibers. Such misdirected fibers may well have contributed to misfunction in early stages; yet this effect could have been eliminated by reeducation before the tic became stabilized.

COMMENT

Man, like experimental animals, may show spasmodic facial twitches or mass contractions after recovery from injury to the facial nerve. The literature contains many descriptions of these, as well as mention of somewhat more unusual, though similar, phenomena observed in man after injury to this nerve: so-called crocodile tears, or paroxysmal

6. Ballance, C., and Duel, A. B.: The Operative Treatment of Facial Palsy by Introduction of Nerve Grafts into Fallopian Canal and by Other Intratemporal Methods, Arch. Otolaryng. **15**:1-70 (Jan.) 1932.

lacrimation during eating (Ford [7]), and abnormal flushing and sweating during eating (Uprus, Gaylor and Carmichael [8]). Recent explanations of all these conditions have invoked some abnormality of the regenerated facial nerve. Thus, Uprus, Gaylor and Carmichael said: "The period of latency between original trauma and onset of symptoms is consistent with an unusual regenerative phenomenon having occurred." Ford interpreted the condition he studied as due to confusion of regenerated vegetative fibers. Spiller [9] offered the idea of total misdirection of regenerating axons as an explanation of the abnormal facial movements. This possibility can neither be affirmed nor denied. However, since there is every reason to believe that tics in man are completely analogous to those observed in monkeys, the presence of branched axons may be assumed in these cases with considerable more assurance.

The present experiments thus offer a new explanation of a well known disorder in man and are interesting clinically because of the light which they shed on the question of prognosis in these cases. In the monkeys the tics showed no diminution over a period of three years, and there was no basis for the belief that any further modification would take place. The tics resulted from a peculiar confusion of peripheral innervation which the simian central nervous system was unable to correct. In man the possibility of totally misdirected axons must be considered. So far as these exist, the tics should show regression, but preponderance of branching axons must greatly limit the possibility of functional adjustment. Here amelioration of a tic may come only through education of the subject in the suppression of the facial movement which carries the tic in its train. In man the prognosis is better than that in monkeys because of the more highly developed inhibitory functions of the human central nervous system. Man, more conscious of appearances than the laboratory animal, obtains a better cosmetic effect through suppression of facial activity.

SUMMARY

1. Anatomic and physiologic studies were made on the facial muscles of twenty-seven rhesus monkeys in which facial paralysis and subsequent recovery had taken place after interruption of the facial nerve.

7. Ford, F. R.: Paroxysmal Lacrimation During Eating as a Sequel of Facial Palsy (Syndrome of Crocodile Tears): Report of Four Cases with Possible Interpretation and Comparison with Auriculotemporal Syndrome, Arch. Neurol. & Psychiat. **29**:1279-1288 (June) 1933.

8. Uprus, V.; Gaylor, J. B., and Carmichael, E. A.: Localized Abnormal Flushing and Sweating on Eating, Brain **57**:443-453, 1934.

9. Spiller, G.: Contracture Occurring in Partial Recovery from Paralysis of the Facial Nerve and Other Nerves, Arch. Neurol. & Psychiat. **1**:564-566 (May) 1919.

2. After an average of forty-four days function began to return in the paralyzed muscles, and after from fifty-two to seventy-nine days purposeless ticlike movements made their appearance. These tics involved various portions of the facial musculature and were synchronous with purposeful movements elsewhere in the facial field.

3. From the demonstration, first, of a phenomenon similar to the axon reflex in the regenerated facial field and, second, of actual branching of axons at the site of injury, it was concluded that single regenerated axons had by branching come to supply widely separated muscles and that an irrevocable functional union had taken place between muscles which do not normally contract simultaneously.

4. The tics which follow injuries to the facial nerve in man are discussed in the light of these observations.

ROENTGENOLOGIC STUDY OF ORIENTATION OF THE PINEAL BODY

I. COMPARISON OF THE PROPORTIONAL AND THE GRAPHIC METHOD IN ABSENCE OF TUMOR OF THE BRAIN

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Since Schüller, in 1918, first emphasized the importance of noting the position of the pineal body in cases of tumor of the brain and cerebral atrophy, increasing significance has been attached to its orientation in cases of intracranial pathologic conditions in which the presence of a mass or destruction or malformation of the brain is suspected. In earlier observations the measurements were readily made, for they were restricted to the anteroposterior or postero-anterior film, determining the midline relationships only. Many pineal glands were not sufficiently calcified to be identified on such films, and at the most such measurements could only lateralize the lesion. Under these circumstances, it was to be expected that attempts would be made to gain further information by the mensuration of the lateral film, and it was fitting that the work should be carried on at the hospital in which Cushing had collected a mass of diagnostic, operative and other data unequaled in scope and throughness.

Vastine and Kinney, pursuing such a study under the direction of Sosman in 1927, described a method which has been used since as a routine by roentgenologists and neurosurgeons. There can be no doubt of the value of the method, which consists in finding the maximum longitudinal diameter from the inner table of the frontal bone to the inner table of the occipital bone and noting the position of the pineal body along this diameter. Normal glands fall within a restricted zone along this plane of the skull. Pineal glands situated in front of or behind this zone are considered displaced. Similarly, normal pineal bodies fall within a restricted zone along the vertical diameter of the skull, obtained by measuring the distance from the inner table of the vertex to the level of the floor of the posterior fossa. In each measurement, the point selected is the one farthest from the pineal body and hence the longitudinal and vertical diameters may not be straight lines, owing to the fact that the pineal body does not always fall along the lines of the maximum anteroposterior and vertical diameters of the skull. When the

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most distant points are connected, the longitudinal diameter is represented by the sum of the distance between the pineal body and the most distant point on the inner table of the frontal bone and the distance of the pineal body from a similar point on the occipital bone rather than by a straight line between the frontal and the occipital bone. As will be seen later, there is little difference in routine work between the two sets of measurements, and it is doubtful whether the slight changes would alter materially the interpretation of results in the average case.

The method of Vastine and Kinney, when analyzed, is merely a graphic expression of their observations that the pineal body falls in a band, or limited zone, along the diameter of the skull under consideration. This band represents a fraction of the total diameter which may be oriented along this plane without difficulty, if the percentile relationships of the distances in front and behind the zone are known. For example, simple computation will show that the anterior border of the normal band lies along a plane from 54 to 57 per cent of the distance between the frontal and the occipital bone (maximum longitudinal diameter), while the posterior border is represented by 61 per cent of this diameter. The absolute measurements of the skull and pineal body are unimportant in themselves. They become significant only when the one is interpreted as a fractional part of the other.

Measurements may be made directly, without the aid of a centimeter rule, after these percentile relationships are identified. Since common fabricated elastic, such as is used in clothing, stretches uniformly throughout its length, a normal zone may be correctly oriented by marking the band or cord of elastic at points 55 and 60 per cent of the distance between the beginning and the end marker and by stretching this elastic localizer so that the beginning, or zero, marker is at the inner table of the frontal bone and the end-point at the occipital bone; the pineal gland either will fall within the zone or, if outside the zone, will lie in front of or behind it, according to its position (fig. 1). The pineal bodies which fall within the zone are interpreted as normal; the others are considered to be displaced anteriorly or posteriorly, as the case may be. Displacements in the vertical plane may be determined in a similar manner. The upper border of the normal zone lies at a point 51 per cent of the distance between the vertex and the floor of the posterior fossa, while its lower border is located at a point 57 per cent of the distance. These percentile relationships, which differ slightly from those of Vastine and Kinney, have been derived from an analysis of the data in a normal series of one hundred and four cases (fig. 2).

In preparing a localizer of this kind, its length should be such that when the elastic is slightly stretched it will just span the smallest skull to be measured. The elastic must always be stretched to some

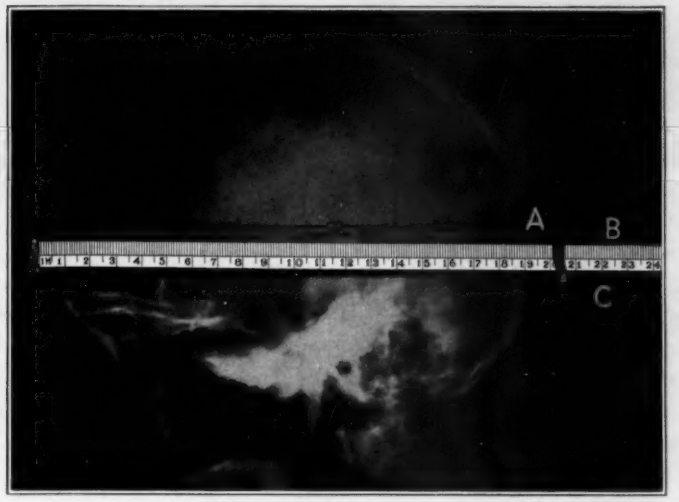

Fig. 1.—Lateral film of the skull of a normal person, showing the manner in which the localizer is employed in the proportional method. The stretched elastic cord (*A*) with the two markers demarcates the normal zone. The calcified pineal shadow is outlined by the oval shadow, with the black dot representing its center. All measurements are made from the central point rather than from the periphery of the pineal shadow. The two markers of the elastic cord for the measurements of the vertical diameter have been removed purposely from the photograph to avoid confusion. The centimeter scale (*B*) has been added to the localizer to permit direct measurements to be obtained for the graphic method, if desired. The pull of the elastic on the collar (*C*) automatically catches the mechanism in any position.

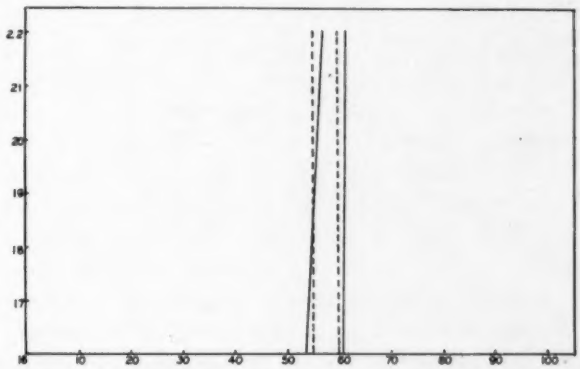

Fig. 2.—Graph illustrating percentile relationships of the normal pineal zone with reference to the anteroposterior diameter of the skull. The values at the abscissas represent percentages of the skull length; the ordinates, the skull length, expressed in centimeters. The normal pineal zone for the proportional method lies between the broken lines, and that for the graphic method, between the solid lines.

extent, even for the smallest skull. Without stretching, false readings will be made. When the band is stretched for the largest skulls, accurate measurements will be obtained, for preliminary experiments have shown that the elastic stretches uniformly for each unit of its length until the practical limit of its elasticity is reached. An elastic band of this type has been used in routine orientation of the pineal body for three years, with properly placed markers to indicate the normal zones for both longitudinal and vertical measurements. It has saved the time required for absolute measurements of the pineal gland and has had the particular advantage of eliminating the need of consulting graphic charts to interpret results.

It should be recognized that the method described by Vastine and Kinney and the proportional method which I devised are not strictly comparable in all respects. While the results obtained by the two procedures are similar in the majority of cases, the methods vary in the following respects: 1. In using the proportional method, the maximum diameter is taken along a straight line between the two points most distant from the pineal body, while in the graphic method of Vastine and Kinney these measurements may or may not be a straight line, depending on the shape of the skull. At the most, this variation in length between the two types of measurements amounts to only a few millimeters. The interpretation of results is not altered materially in the average case. 2. The width of the normal zone is constant in the method of Vastine and Kinney, while in our method the width of the zone varies with the size of the skull; i. e., in the first method the width of the normal zone is 1 cm. for a small skull measuring 17 cm. in its anteroposterior diameter and also for a long skull measuring 22 cm. This relationship is graphically illustrated in charts of these authors by the parallelism of the lines representing the anterior and posterior borders of the normal zones. In the proportional method the width of the normal zone will be narrower in small skulls with a short anteroposterior diameter and wider in the long skulls. This leads to greater accuracy, decreasing the number of false normals. 3. On comparing the absolute figures of the graph obtained by the method of Vastine and Kinney (fig. 3) with percentile measurements, one finds that the anterior border of the normal zone for the shortest skulls falls at a point which is approximately 54 per cent of the total anteroposterior diameter, while for the longest skulls this border falls at a point 57 per cent of this diameter. This indicates that for a long skull the pineal body to be interpreted as normal must lie farther posteriorly within the cranium, not only in absolute measurement but in terms of the percentile length of the cranium. Computation shows that the position of the posterior border does not vary materially in the per-

centile relationships, remaining approximately 61 per cent of the anteroposterior diameter, and is independent of the length of the skull. In the method of Vastine and Kinney there obtains the unusual result that one of the two borders of the normal zone varies in its percentile relationships while the other does not. With the elastic method the position of both borders varies strictly according to these proportional relationships.

Because of these differences, variations may be expected in borderline cases, particularly in those in which the pineal body falls at the anterior border of the normal zone. It should be remembered that in dolichocephalic skulls normally the pineal body is not frequently shown anterior to the normal zone when the method of Vastine and Kinney is employed. The reason for this immediately becomes apparent when the percentile relationships of the normal zone are studied (fig. 3). For a skull of 22 cm. in length, the position of a normally placed

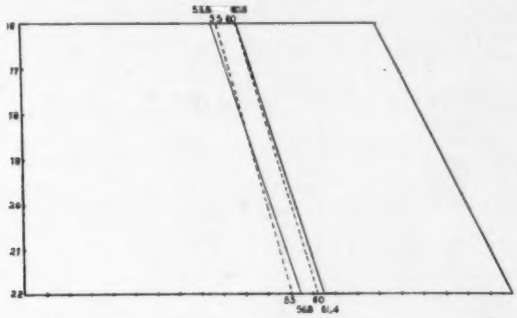

Fig. 3.—Graph of anteroposterior measurements, expressed in absolute units, comparing the proportional and the graphic method. The normal zone for the proportional method lies between the broken lines, and that for the graphic method, between the solid lines. The solid lines run parallel, indicating that the width of the normal band by the graphic method does not change with the size of the skull; i. e., it is as wide for a skull with an anteroposterior diameter of 16 cm. as for one of 22 cm. (indicated on the ordinates). In the proportional method the normal band lies anterior to (to the left of) the band of the graphic method for the larger skull lengths. The values at the upper and lower margins of the graph represent percentages of the total anteroposterior diameter, defining the position of the margins of the normal zones by the two methods.

pineal body may vary from 56.8 to 61.4 per cent of the maximum anteroposterior diameter, a total of 4.6 per cent, while for a short skull the normal range is considerably longer—from 53.8 to 60.6 or 6.8 per cent. In our experience, this is the chief factor in the graphic method concerned in producing the error of false normals—misinterpretation of a normally placed pineal body in a long skull as anterior displacement.

One hundred and four cases in which the pineal body was normal have been analyzed, with comparison of the two methods and classification according to orientation (1) outside the normal zone, (2) at the margins of the normal zone or (3) within the normal zone. The distribution was outside the normal zone in seventeen, or 16.3 per cent, of the one hundred and four cases when the graphic method was employed and in eight, or 7.7 per cent, when the proportional method was used. This represents a reduction of approximately 50 per cent in the number of false normals. The number of cases in which the pineal body was marginal was reduced slightly, from twenty-one (20 per cent) to eighteen (17.3 per cent). The number of cases in which the pineal body fell within the normal zone, exclusive of those in a marginal position, was increased from sixty-six (63.4 per cent) to seventy-eight (75 per cent). When pineal bodies which were located at the margin

TABLE 1.—*Pineal Localization with Reference to the Anteroposterior Diameter, With Comparison of Variations in the Graphic and Proportional Methods in One Hundred and Four Cases of a Normal Pineal Body*

Anteroposterior Diameter of Skull, Cm.	Number of Cases	Number of Pineal Glands Anterior to Normal Zone		Number of Pineal Glands at Anterior Margin		Number of Pineal Glands in Normal Zone		Number of Pineal Glands at Posterior Margin		Number of Pineal Glands Posterior to Normal Zone	
		Graphic	Proportional	Graphic	Proportional	Graphic	Proportional	Graphic	Proportional	Graphic	Proportional
18-19	18	0	0	1	1	16	13	0	2	0	1
19-20	36	4	2	6	2	25	27	0	3	1	2
20-21	38	7	2	9	3	22	27	0	6	0	0
21-22	11	4	0	5	1	2	10	0	0	0	0
22-23	2	1	1	0	0	1	1	0	0	0	0
Total	104	16	5	21	7	66	78	0	11	1	3

are included in the normal series, 83.7 per cent may be classified as normal by the graphic method and 92.3 per cent by the proportional method. The errors in the graphic method do not arise as a result of the pineal body falling posterior to the normal zone in many instances. In fact, remarkably few were so distributed. The error arises in the main as a result of the number of pineal bodies which fell anterior to this zone. In an analysis of this series, no errors of this type were observed in skulls with a very short anteroposterior diameter (from 18 to 19 cm.), while there were four false normals in thirty-six skulls (11 per cent) with an anteroposterior diameter of from 19 to 20 cm., seven in thirty-eight skulls (18 per cent) with a diameter of from 20 to 21 cm., four in eleven skulls (36 per cent) with a diameter of from 21 to 22 cm. and one in two skulls (50 per cent) with a diameter of from 22 to 23 cm. (table 1). The increase in false normals becomes apparent at once when the data are subjected to such an analysis. An error of this type is greatly reduced when the proportional method is

employed. An illustration of this error, with a comparison of the two methods, is shown in figure 4.

In considering the vertical diameter of the skull, the normal zones for the graphic and proportional methods are found to present differences in width and position. These differences are best analyzed by means of a diagram (fig. 5). In general, it may be stated that these differences are similar to those observed with reference to the anteroposterior diameter of the skull and need no further consideration at this time.

The distribution of the pineal bodies along the vertical diameter of the skull as determined by the graphic and proportional methods is shown in table 2. Variations within a range of from 51 to 57 per cent, inclusive, were accepted as normal for the proportional method. The

TABLE 2.—*Variations in Pineal Localization with Reference to the Vertical Diameter of the Skull, with Comparison of the Graphic and Proportional Methods in One Hundred and Four Cases of a Normal Pineal Body*

Vertical Diameter of Skull, Cm.	Number of Cases	Number of Pineal Glands Above Normal Zone		Number of Pineal Glands at Superior Margin		Number of Pineal Glands in Normal Zone		Number of Pineal Glands at Inferior Margin		Number of Pineal Glands Below Normal Zone	
		Graphic	Proportional	Graphic	Proportional	Graphic	Proportional	Graphic	Proportional	Graphic	Proportional
14-15	26	1	1	1	4	24	18	0	3	0	0
15-16	38	2	1	5	2	30	30	1	2	0	1
16-17	35	3	0	7	2	25	30	0	2	0	0
17-18	5	3	1	0	1	2	3	0	0	0	0
Total	104	9	3	13	9	81	81	1	7	0	4

pineal body was found to lie above the normal zone in nine of the one hundred and four cases (9 per cent) by the graphic method and in three cases (3 per cent) by the proportional method. It was noted below the normal zone in none of the cases by the graphic method and in four cases by the proportional method. The total number of cases of marginal localization varied little in the two methods, though in more cases the pineal body was noted at the superior margin by the graphic method and at the inferior margin by the proportional method. The number of instances in which the pineal gland fell within the normal zone was the same in the two series (81, or 77.9 per cent).

The incidence of errors in the two methods was also correlated with the index of the skull obtained by the formula $\frac{\text{vertical diameter of skull}}{\text{longitudinal diameter of skull}} \times 100$. This index is of such a character that skulls with a high vertex or a low occipital floor will show a higher index than those with a low vault and a relatively long anteroposterior diameter. It will be noted that

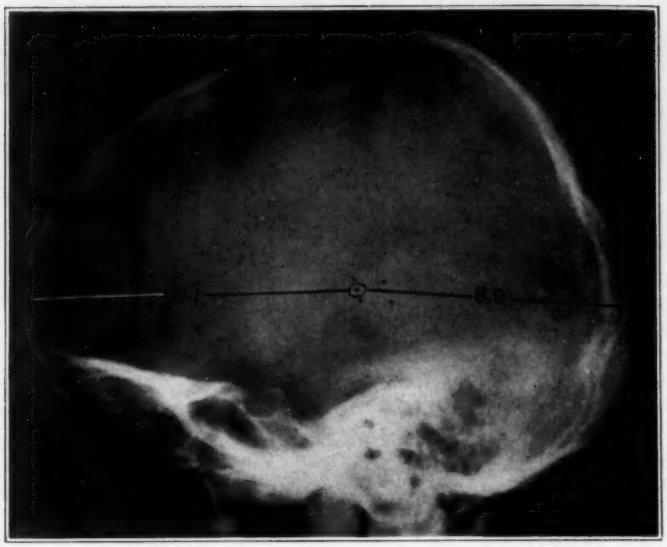

Fig. 4.—Anteroposterior measurements of a normal skull with a high vault. The pineal body in this case (the central point of the calcification) should lie within the two lower dots to be in normal position by the graphic method. The upper dots show the zone for the proportional method. In all illustrations the lines of the anteroposterior diameter stop at the margins of the pineal body, to avoid confusion. The measurements in every instance were actually made from the central point of the pineal body, and the figures in all illustrations represent the true values for such measurements.

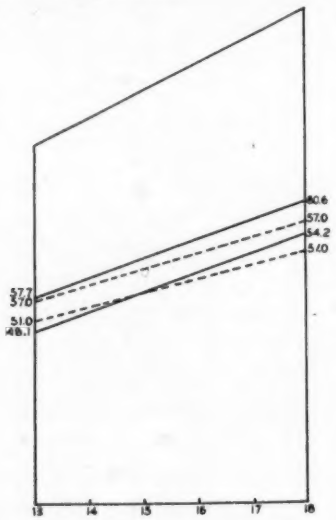

Fig. 5.—Graph of vertical measurements, expressed in absolute units comparing the proportional and the graphic method. The normal zone for the graphic method lies between solid lines, and that for the proportional method, between incomplete lines. The normal zone by the graphic method does not change in width with the size of the skull, and that by the proportional method lies slightly lower in a skull with a long vertical diameter. The values at the side of the graph demarcating the normal zones are percentages of the total vertical diameter; i. e., the upper normal limit for a skull with a vertical diameter of 13 cm. is 57.7 per cent of the diameter by the graphic method and 57 per cent by the proportional method.

the number of pineal bodies falling either anterior or superior to the normal zone is correlated with this index, such positions being observed most commonly in skulls with a low vault (relatively large anteroposterior diameter) and a low occipital floor at the posterior fossa (relatively high vertical diameter), respectively. When the graphic method is employed, the number of skulls in which the pineal body is shown anterior to the normal zone becomes smaller as the index of the skull increases. The number of cases in which the pineal body is anterior to the normal zone is much less when the proportional method is used. In all of the five cases in this series an index below 80 was presented. The incidence of pineal bodies located above the normal zone (by the graphic method) is correlated positively with a high skull index.

In summarizing the findings, it may be stated that in practice both the graphic and the proportional method fail to identify the normal position of the pineal body in all cases. The errors are materially decreased by the use of the proportional method. In particular, it eliminates erroneous interpretation of the position of normally situated pineal bodies which are found to be located anterior to the normal zone by the graphic method. These errors have been found to be related to the shape of the skull and are not restricted to dolichocephalic skulls but occur for skulls with an unusually high vault or a low floor at the posterior fossa.

SUMMARY

A simple method of localization of the pineal body has been devised which is based on strict proportionality of the measurements of the anteroposterior and the vertical diameter of the skull.

The results of this method have been compared with those obtained by the graphic method in a series of one hundred and four cases of a normal pineal body.

The incidence of false normals was reduced materially by the use of the proportional method, particularly in respect to normal pineal bodies located anterior to the normal zone.

An analysis of errors indicates a relationship between the incidence of false normal and the skull index obtained by dividing the vertical diameter by the longitudinal diameter of the skull.

A CLINICOPATHOLOGIC STUDY OF ASTROCYTOMAS

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AND
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ANN ARBOR, MICH.

The biologic character of the astrocytoma is little known, although this neoplasm has been treated surgically with some success. Astrocytomas of the cerebrum can be divided into two groups—the bilateral and the unilateral. We wish to demonstrate that it is possible to determine the laws of growth of this tumor and the factors responsible for the bilateral invasion, since the astrocytoma invades and follows the myelinated tracts. Bilateral invasion occurs regularly when the tumor originates in the corpus callosum.

This investigation is limited to astrocytoma of the cerebrum, excluding that of the cerebellum, which represents a different type. The macroscopic study was most important. Weigert sections were used to demonstrate the type and extent of the neoplasm. Histologic examination was valuable in the differentiation of demyelinization resulting from tumor and that produced by edema. Twelve cases will be described.

From the clinical standpoint few definite conclusions can be drawn, and this study will be devoted mainly to discussion of the pathologic features.

REPORT OF CASES

BILATERAL ASTROCYTOMA

CASE 1.—D., a woman aged 45, complained of headaches and fatigue four months before admission to the hospital. Examination revealed emotional dulness, fatigability, moderate loss of memory, bitemporal, occipital and frontal headaches and inconstant tinnitus. The right pupil was larger than the left, and there was weakness of the right side of the face. The visual fields showed moderate concentric contraction. The tendon reflexes were more active on the right than on the left. There were Hoffmann's sign, bilateral ankle clonus, astereognosis on the right, bilateral ataxia in the finger to nose test and weakness with some spasticity of both lower extremities. The pressure of the spinal fluid was 90 mm. of water, and the fluid contained 81 mg. of sugar per hundred cubic centimeters; there was 88 mg. of sugar per hundred cubic centimeters of blood. Roentgen examina-

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tion of the skull, a ventriculogram and subsequent subtemporal decompression failed to reveal any evidence of tumor. The patient died after operation, without regaining consciousness.

Pathologic Observations.—The brain was normal in size and appearance but very hard in consistency, the cut section appearing snow white. The outlines of the tumor could not be defined in unstained material.

Weigert sections through the anterior part of the frontal lobes and the genu of the corpus callosum (fig. 1 *A*) showed that the latter was greatly thickened and its myelin diffusely reduced. The corona radiata on both sides was demyelinated and wider than normal. Sections through the midpart of the striatum showed considerable but even enlargement and moderate demyelinization. The corona radiata on both sides was distinctly demyelinated, more so on the left. There were also demyelinization in the internal capsules and moderate reduction of myelin in the pallidum, septum pellucidum and fornix. The most pronounced demyelinization was seen in a section through the midpart of the thalamus (fig. 1 *B*). Here the corpus callosum, the thalamus and external capsule on both sides and the white matter of the parietal lobes were considerably demyelinated. The temporal lobes were normal. In the posterior part of the parietal lobes demyelinization decreased rapidly, and the occipital lobes, as well as the posterior fourth of the corpus callosum, were normal.

Interpretation.—The thickening and demyelinization of the anterior half of the corpus callosum suggested that the nucleus of the tumor was in its anterior part; from here tumor cells grew bilaterally into the corona radiata and the internal capsule, invading both hemispheres to about the same extent. The bilateral invasion of the thalamus and pallidum, since both are rich in myelin, represented a direct continuation of the tumor. The involvement of the septum pellucidum and the fornix was an extension from the corpus callosum. The path of invasion of the tumor through the external capsule appeared to have been interrupted by the striation of the uncus because of the difference in direction of the fibers. Thus, the main tumor was encountered in the anterior part of the corpus callosum, the frontal and parietal lobes, the insulae, the capsulae internae and the basal ganglia. The occipital and temporal lobes, the brain stem and the cerebellum were spared.

Case 2.— R., a man aged 50, complained of convulsions, headaches and diplopia three and one-half years before admission to the hospital. He noticed paresthesias of the left hand preceding the convulsions. These attacks were at first focal and then became generalized. At the time of his admission to the hospital he was deteriorated mentally. The left pupil was larger than the right, but the eyegrounds were normal. There were left hemiparesis with involvement of the face and forced grasping; astereognosis was noted on the left. There were precipitate micturition and occasional incontinence. The spinal fluid was normal. Roentgen examination of the skull gave normal results. An encephalogram revealed no filling of the right ventricle. A presumptive diagnosis of a right frontoparietal lesion was made, which was confirmed by a ventriculogram. Subtemporal decompression was performed, and a part of the tumor was removed. The patient died without regaining consciousness.

Pathologic Observations.—Sections through the genu of the corpus callosum showed advanced demyelinization and thickening of the genu, but a normal rostrum (fig. 2 *A*). There was advanced demyelinization in the left frontal lobe and, to a lesser extent, in the right frontal lobe, which had been partly removed by the

surgeon. The anterior half of the corpus callosum was thickened and demyelinated (fig. 2*B*). Section through the basal ganglia revealed pronounced demyelinization in the gyrus cinguli on both sides, more so on the right, the right parietal

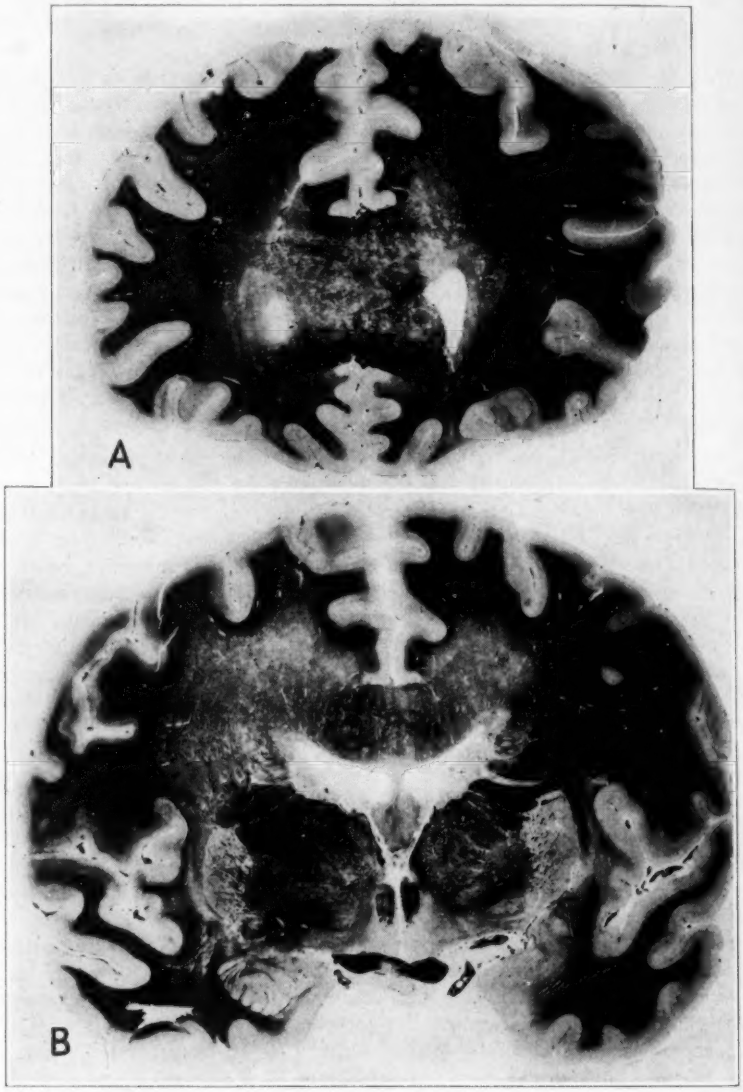

Fig. 1.—Sections with Weigert stain. *A* (× ¾) is through the frontal lobes, showing thickening and demyelinization of the corpus callosum and considerable demyelinization of the corona radiata, and *B* (× ½), through the middle part of the thalamus, showing great thickening and demyelinization of the corpus callosum and considerable demyelinization of the parietal lobe, internal capsule and thalamus on both sides.

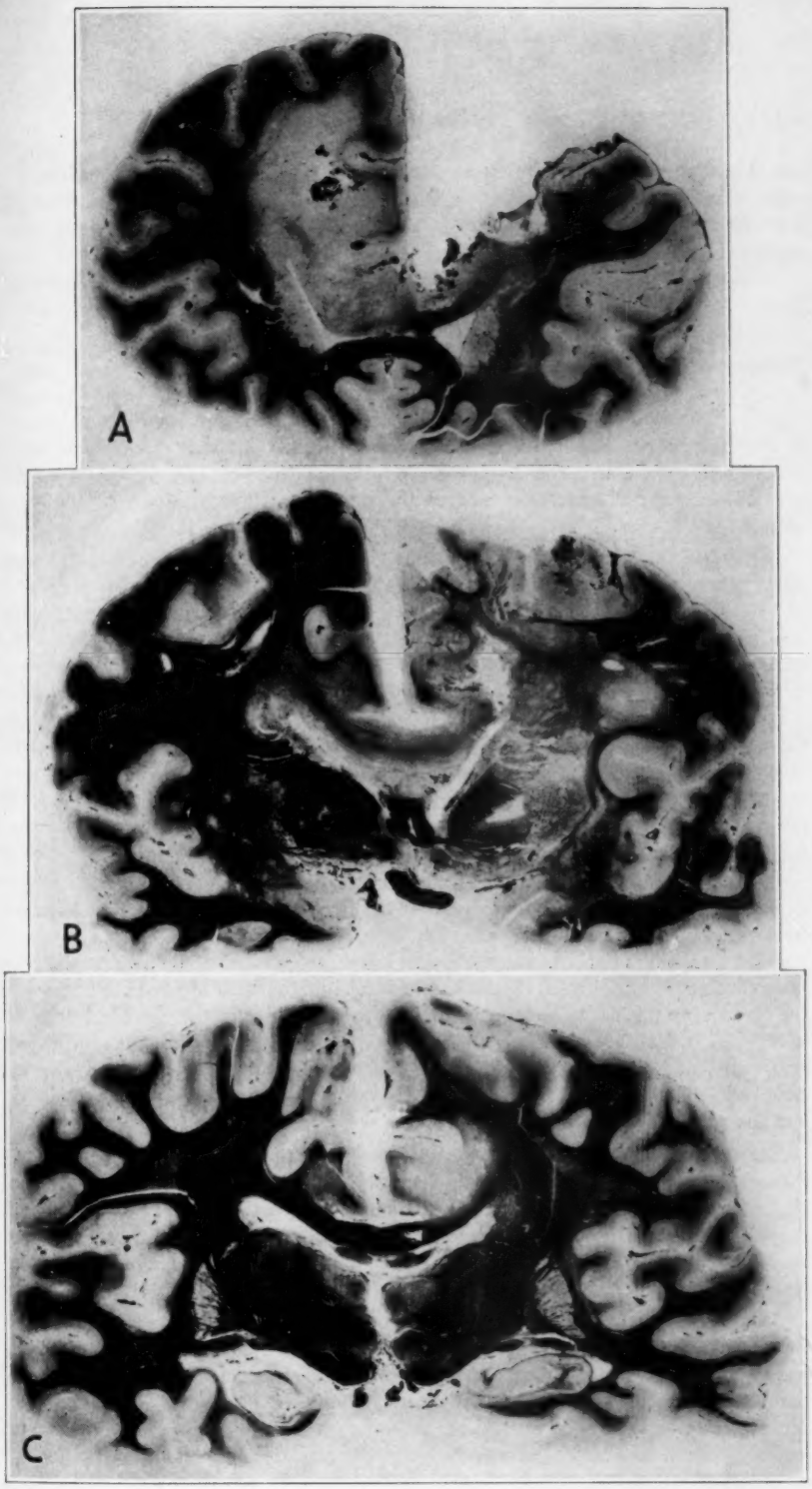

Fig. 2.—Sections (Weigert stain; × ½) showing (*A*) demyelinization of the genu of the corpus callosum and the left frontal lobe, with a large part of the right frontal lobe removed; *B*, demyelinization of the corpus callosum, the right parietal lobe, the right internal capsule and both gyri cinguli, and *C*, with a surgical defect in the right parietal lobe, the thalamus, in which the corpus callosum is normal and there is demyelinization in the gyrus cinguli on both sides, more so on the right.

lobe and the right capsula interna. Moderate demyelinization was present in the right capsula externa. Sections through the midpart of the thalamus revealed that the corpus callosum was normal in width and myelin content (fig. 2*C*). The gyrus cinguli was demyelinated, on both sides, more so on the right. A few millimeters occipitally from this section there was no demyelinization. The posterior half of the corpus callosum, both temporal and both occipital lobes, the basal ganglia, the brain stem and the cerebellum were normal.

Interpretation.—The thickening and demyelinization of the genu of the corpus callosum associated with pronounced invasion of both frontal lobes suggested that the nucleus of the tumor was in the genu. The distribution of the tumor in the frontoparietal region was somewhat asymmetrical, the invasion being more pronounced on the left and involving the white matter near the convexity of the frontal and parietal lobes. Invasion of the right internal capsule and of the basal ganglia was limited.

CASE 3.—D., a man aged 33, complained of headaches five years before admission to the hospital. Later, loss of memory and progressive mental deterioration developed. At the time of admission to the hospital there was slight expressive aphasia; the left pupil was larger than the right, and there was weakness on external rotation of the eyes to the right. There were choked disks of 4.5 diopters, with hemorrhages. The knee jerk was more active on the left than on the right. Examination of the blood and urine revealed nothing abnormal. The pressure of the spinal fluid was 360 mm. of water, but there was no increase in solids. Roentgen examination of the skull showed erosion of the pituitary fossa; an encephalogram revealed no air in the ventricles. The patient became comatose six hours after encephalography. Operation was performed; death occurred two hours later.

Pathologic Observations.—The anterior part of the corpus callosum was greatly thickened and demyelinated, and there was advanced demyelinization bilaterally in the frontal and parietal lobes, the thalamus, the internal capsule and the parolfactory area. More posteriorly the corpus callosum was moderately demyelinated; the parietal lobe, the basal ganglia, the internal and external capsules, the fasciculus uncinatus and the adjacent white matter of the temporal lobe on both sides were severely demyelinated (fig. 3). The demyelinization decreased occipitally, and the white matter of both occipital lobes was normal. However, histologic examination revealed tumor cells in the occipital lobes, the midbrain and the pons. The medulla and cerebellum were free from tumor cells.

Interpretation.—The thickening and demyelinization of the anterior part of the corpus callosum associated with demyelinization of both frontal and parietal lobes suggested that the nucleus of the tumor was in the anterior half of the corpus callosum. The tumor elements streamed into the corona radiata, the centrum semiovale and the basal ganglia and reached the midbrain through the pyramidal tracts.

CASE 4.—E., a woman aged 50, complained of depression and mental confusion fourteen months before admission to the hospital. She had frequent crying spells and experienced pain in the occipital region. After ventriculography the symptoms improved for eight months. Six months before her admission to the hospital the patient complained of increasing difficulty in the use of the right arm and leg, and the mental state became worse. Examination disclosed retardation of thought and emotional lability. There was weakness of the right side of the face, the right arm and the right leg. The reflexes were overactive on both sides, and

there were suggestive Oppenheim and Gordon signs on the right. The patient walked with a right hemiparetic gait. There were choked disks of 1 diopter, with hemorrhages. Spinal puncture was not performed. Roentgen examination of the skull revealed nothing abnormal. Left frontoparietal craniotomy was performed, but no tumor was observed. Death occurred twenty-four hours after the operation.

Pathologic Observations.—The brain was larger than normal and firm in consistency; the convolutions were moderately flattened. Frontal sections revealed that the entire corpus callosum was greatly thickened and demyelinated and that there was diffuse, uniform demyelinization of both hemispheres, the basal ganglia, the internal capsules and the right side of the basilar part of the pons (fig. 4). The cerebellum was normal.

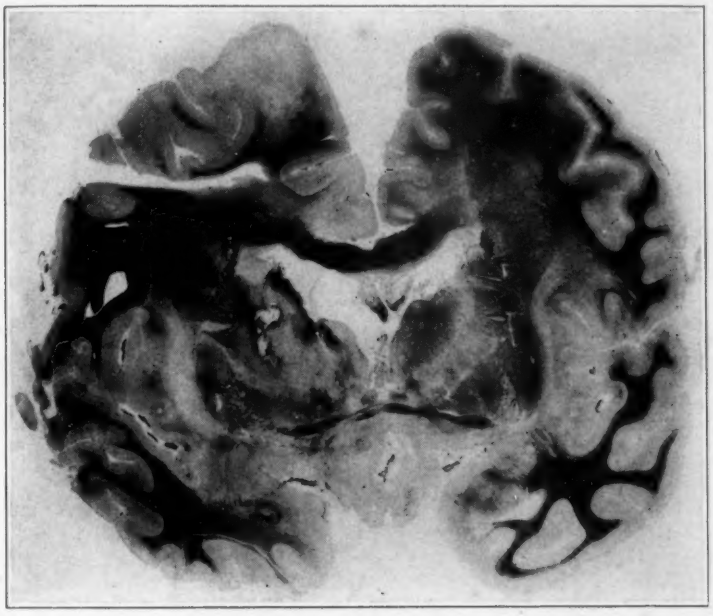

Fig. 3.—Advanced demyelinization of the basal ganglia, parietal lobe, external capsule and parolfactory area bilaterally. Weigert stain; × ½.

Interpretation.—Involvement of the entire corpus callosum was responsible for the general invason of both hemispheres and the brain stem.

Case 5.—McM., a man aged 26, complained of "throbbing headaches occurring in the morning," projectile vomiting, loss of vision, somnolence and loss of memory one year before admission to the hospital. Examination revealed almost constant tinnitus, questionable superior right homonymous quadrantanopia, bilateral weakness of the sixth nerve, vertical and horizontal nystagmus, weakness of the right side of the face and choked disks of 6 diopters. The biceps and triceps reflexes were more active on the right than on the left. The knee jerks were hyperactive but equal. There was no definite astereognosis, although the patient had difficulty in recognizing some objects in both hands. There was swaying in the Romberg

position, both with the eyes open and with the eyes closed. The Bárány test gave normal results. The pressure of the spinal fluid was 460 mm. of water on ventricular tap. Lumbar puncture was not performed. Roentgen examination of the skull disclosed evidence of increased intracranial pressure. Suboccipital craniotomy was performed; the patient died twenty-four hours later.

Pathologic Observations.—The brain was larger than normal; the gyri were wide, especially those of the left temporoparietal region. Frontal sections revealed that the splenium of the corpus callosum was greatly thickened and demyelinated. There was far advanced demyelinization of both occipital lobes, the posterior parts of both parietal lobes and the left temporal lobe. The anterior half of the corpus callosum was of normal width and myelin content (fig. 5). The posterior two thirds of the posterior limb of the internal capsule was demyelinated bilaterally,

Fig. 4.—Thickening and demyelinization of the corpus callosum, associated with diffuse demyelinization of the hemispheres and the basal ganglia. Weigert stain; × ½.

but more so on the left (fig. 5). Demyelinization of the hemispheres gradually diminished in the anterior part of the parietal lobe. The myelin of both frontal lobes was well preserved, although histologic examination revealed numerous tumor cells in this region. In the basal ganglia and the midbrain were numerous tumor elements, but none were observed in the cerebellum. Tumor cells were present in the perivascular spaces.

Interpretation.—The thickening and demyelinization of the splenium of the corpus callosum associated with marked demyelinization of the occipitotemporal region suggested that the nucleus of the tumor was in the splenium or the posterior half of the corpus callosum. The growth of the tumor followed the pathways of the major forceps as far as the uncus and the cornu ammonis. The tapetum and fasciculus longitudinalis inferior gave easy access to the temporal lobes and the posterior parts of the internal capsule.

UNILATERAL ASTROCYTOMA

CASE 6.—C., a man aged 28, complained of "fainting attacks" followed by convulsions, severe headaches and tinnitus for twenty-eight months before admission to the hospital. These attacks came without warning; they were associated with hypertonicity, frothing at the mouth and clonic movements of all extremities and were followed by weakness of the left hand and arm. Examination revealed choked disks of from 1 to 2 diopters and astereognosis and hemiparesis on the left. The reflexes were hyperactive on the left, except the abdominal reflexes, which were absent. Hoffmann's sign was elicited on the left. The pressure of the spinal fluid was 510 mm. of water when the patient was in the upright position. Roentgen examination of the skull revealed nothing abnormal. An encephalogram indicated a right frontoparietal lesion. Right temporal craniotomy was

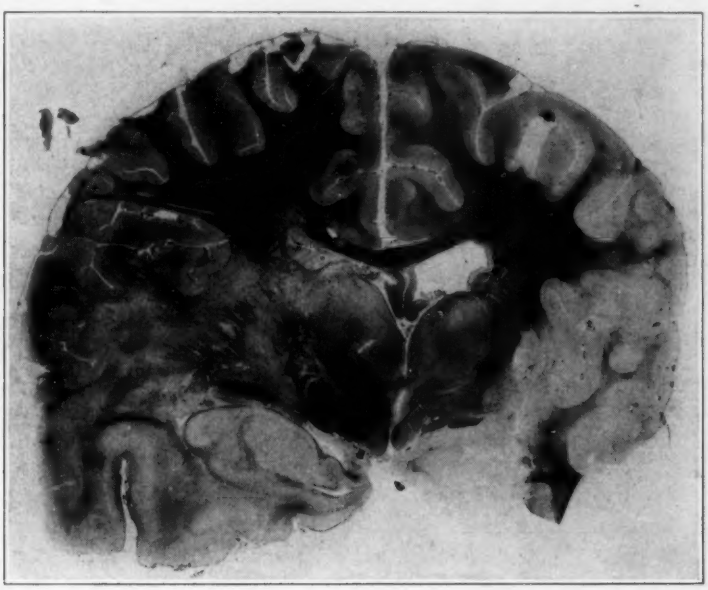

Fig. 5.—Advanced demyelinization of the temporal lobe and the thalamus on both sides, more so on the left. The corpus callosum is normal. Weigert stain; × ½.

performed, and a part of the tumor was removed. The patient was placed on a dehydration regimen. Three months later the symptoms recurred, and a second operation was performed, with relief of the symptoms for fifteen months, after which a third operation was performed; the patient died several hours later.

Pathologic Observations.—The myelin of the entire right parietal lobe and of the adjacent parts of the frontal and occipital lobes was destroyed. There were moderate invasion of the right thalamus and beginning extension of the tumor into the corpus callosum. The brain stem and cerebellum were normal (fig. 6). A large part of the right parietal lobe and the insula had been removed surgically.

Interpretation.—Advanced demyelinization of the right parietal lobe suggested that the nucleus of the tumor was in that region. The invasion of the corpus

callosum occurred late, the opposite hemisphere remaining free. Repeated operations resulting in the destruction of large parts of the lobe rendered further interpretation difficult.

CASE 7.—The clinical history in this case was not available.

Pathologic Observations.—The right hemisphere was larger than the left, and the convolutions were flattened. Frontal sections through the midpart of the parietal lobes revealed advanced demyelinization of the parietal and temporal lobes on the right and the basal ganglia (fig. 7). The adjacent parts of the frontal and occipital lobes were demyelinated, but their tips were normal. There was prolapse of the right parietal lobe, caused by decompression. The midpart of the corpus callosum was greatly thickened and demyelinated. The left hemisphere was compressed, but there was no demyelinization. The brain stem and cerebellum were normal. There were tumor elements in the perivascular spaces.

Fig. 6.—The right parietal lobe is demyelinated and partly destroyed, and a large surgical defect appears in the right insula. There is beginning extension of the tumor into the corpus callosum. The left hemisphere is normal. Weigert stain; × ½.

Interpretation.—Severe destruction of the right basal ganglia and the right parietal lobe suggested that the nucleus of the tumor was in the basal ganglia, with subsequent radiation into the white matter of the right parietal lobe. Invasion of the corpus callosum apparently occurred late, the left hemisphere consequently remaining free. Invasion of the perivascular spaces is possibly responsible for the irregular distribution of the tumor.

CASE 8.—H., a man aged 32, complained of headache, generalized convulsions and progressive loss of vision two years before admission to the hospital. Examination revealed choked disks of 4 diopters, mild right hemiparesis, increased tendon reflexes and diminished umbilical reflexes on the right. Roentgen examination of the skull revealed nothing abnormal. The pressure of the spinal fluid was 170

mm. of water, and the fluid contained 6 cells. The diagnosis of a neoplasm in the left posterior frontal region was made. The patient died suddenly, before operation could be performed.

Pathologic Observations.—Sections through the midpart of the right temporal lobe showed complete demyelinization of the entire lobe, most pronounced in the area of the nucleus amygdalae (fig. 8). The substantia perforata anterior was demyelinated on both sides. There was moderate demyelinization of the right thalamus, the adjacent part of the internal capsule, the fasciculus uncinatus, the capsula externa and the capsula extrema. Histologic examination disclosed tumor cells in the brain stem.

Interpretation.—The origin of the tumor was in the nucleus amygdalae, from which it invaded the cerebral peduncle, the anterior part of the thalamus and the

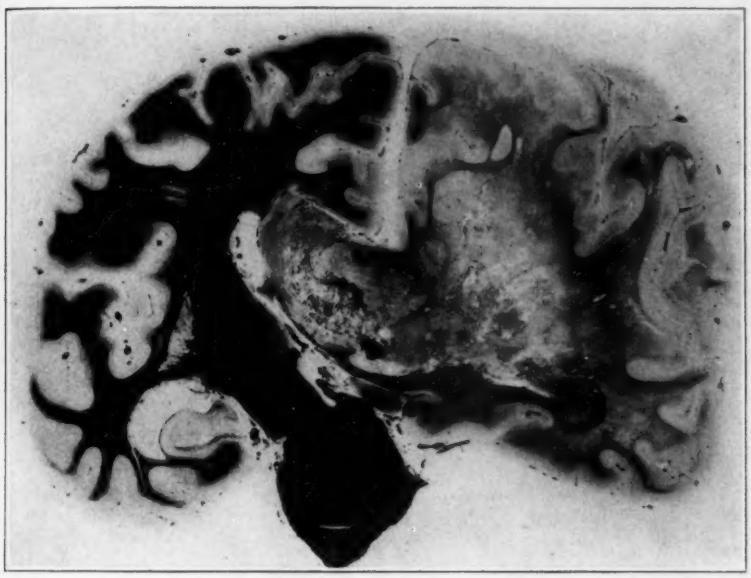

Fig. 7.—Advanced demyelinization of the right parietal and temporal lobes, the basal ganglia and the corpus callosum. The left hemisphere is compressed but is not invaded by the tumor. Weigert stain; × ½.

fasciculus longitudinalis inferior. Demyelinization stopped in the fasciculus arcuatus. The tumor cells crossed to the left hemisphere through the fasciculus inferior thalami and the tuber cinereum, infiltrating the fasciculus inferior thalami and the nucleus amygdalae on the left side. An important feature was the invasion of the brain stem through the right pyramidal tract.

Case 9.—W., a woman aged 28, complained of dizzy spells, sick headaches, generalized convulsive attacks and temper tantrums followed by periods of disorientation and confusion six months before admission to the hospital. Examination revealed inequality of the pupils, the left being larger than the right, bilateral weakness of the sixth nerve and paralysis of the seventh nerve on the left. The margins of the disks were blurred, but there was no choking. Vibratory sense was diminished on the left. The gait was weak and ataxic. The Romberg

sign was positive. The patient expressed paranoid ideas and had auditory hallucinations and outbursts of unmotivated laughter and crying. The pressure of the spinal fluid was 160 mm. of water, and the fluid contained 10 cells. The sugar contents of the blood and spinal fluid were 115 and 88 mg., respectively, per hundred cubic centimeters. An encephalogram showed evidence of a left temporosphenoid lesion. Part of the left temporal lobe was removed, and the patient was greatly improved. A year later the symptoms recurred; the patient died after a generalized convulsive attack, before operation could be performed.

Pathologic Observations.—The tumor involved the entire left temporal lobe, completely destroying its myelin and producing extensive necrosis (fig. 9). The tumor further invaded the optic striation and the median surface of the left

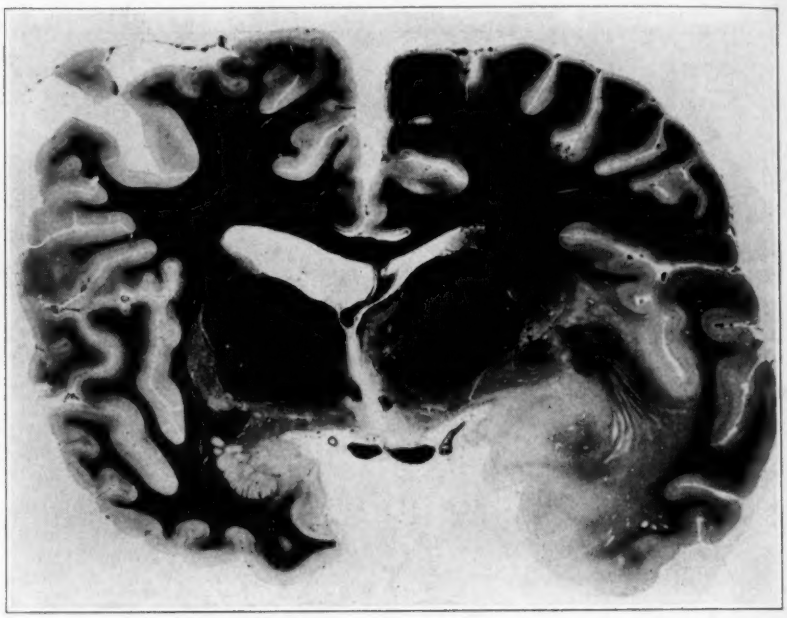

Fig. 8.—Demyelinization of the temporal lobe and substantia perforata anterior on the right. Weigert stain; × ½.

occipital lobe, reaching the calcarine area. The right hemisphere, the brain stem and the cerebellum were not affected. There were tumor elements in the perivascular spaces.

Interpretation.—Because of the extensive destruction of tissue, the invasion of the perivascular spaces and faulty (horizontal) sectioning of the brain, it was impossible to locate the nucleus of the tumor.

Case 10.—De L., a man aged 36, complained of convulsive attacks followed by amnesia and headache for eight years. These attacks began after a severe trauma, accompanied by unconsciousness which lasted two hours. The convulsions were preceded by an olfactory aura and had increased in frequency but decreased in severity. Examination revealed slight weakness of the right lateral rectus muscle and nystagmus on rotation of the eyes to the right. There were choked disks of

3 diopters, with hemorrhages. The pressure of the spinal fluid was 300 mm. of water. Roentgen examination of the skull revealed nothing abnormal. A ventriculogram suggested a tumor of the right temporal lobe. The patient died on the following day, before operation could be performed.

Pathologic Observations.—The bulk of the tumor occupied the uncus and cornu ammonis on the right, both formations being greatly enlarged and completely demyelinated (fig. 10). There was also far advanced demyelinization in the tapetum and thalamic radiation; the fasciculus longitudinalis inferior was partly preserved. The posterior part of the fornix and a limited area of the

Fig. 9.—Complete demyelinization and advanced necrosis of the left temporal lobe. Weigert stain; × ½.

splenium of the corpus callosum were moderately demyelinated. Large areas of the white matter of the temporal lobe and part of the corona radiata were considerably demyelinated. The convexity of the lobe was well preserved. Thus, demyelinization was most pronounced in the gyrus hippocampi and gyrus fusiformis, involving also a part of the median surface of the occipital lobe and gradually disappearing in the posterior part of the fissura collateralis. The basal ganglia, brain stem and cerebellum were normal.

Interpretation.—The tumor arose in the uncus or the cornu ammonis, invading the tapetum and the thalamic radiation but showing little tendency to grow into the fasciculus longitudinalis inferior. The development of the tumor was restricted

to the base and median surface of the temporal lobe and to limited parts of the occipital lobe, sparing the convexity and the brain stem.

CASE 11.—N., a man aged 32, complained of headaches, retardation in thinking and loss of memory for one year before admission to the hospital. Examination revealed that the pupils reacted poorly to light and that the left pupil was larger than the right. There was horizontal nystagmus, which was more marked on looking to the left. There were choked disks of 4 diopters and hemorrhages. There was weakness of the sixth nerve bilaterally. The grip was weaker on the right. The knee jerk was more active on the right. The spinal fluid was not examined. Roentgen examination of the skull showed evidence of tumor of the brain, with erosion of the sella turcica. A ventriculogram indicated a tumor in the right frontal lobe. Part of the tumor was removed, and roentgen treatment was administered. The patient was greatly improved. Six months later he returned with a draining sinus at the operative site, but there were no neurologic symptoms.

Fig. 10.—Complete demyelinization and thickening of the gyrus hippocampi and gyrus fusiformis on the right. There is considerable demyelinization of the white matter of the right temporal lobe. Weigert stain; × ½.

The diseased bone was removed; two weeks later abscess of the brain developed, and the patient died.

Pathologic Observations.—The right frontal lobe was demyelinated. The anterior part of the corpus callosum and the white matter of the left frontal lobe were partly destroyed by the abscess. The internal capsule was of normal myelin content bilaterally (fig. 11). There was moderate demyelinization of the anterior part of the right capsula externa.

Interpretation.—The uniform involvement of the right frontal lobe suggested that the nucleus of the tumor was in the tip of the lobe, from which the growth extended into the genu of the corpus callosum, without as yet affecting the opposite side, and into the capsula externa. This case represents an early stage of development of the astrocytoma.

CASE 12.—L., a man aged 43, complained of nocturnal headaches, nervousness, tremor of the hands, increased irritability, loss of memory and loss of vision

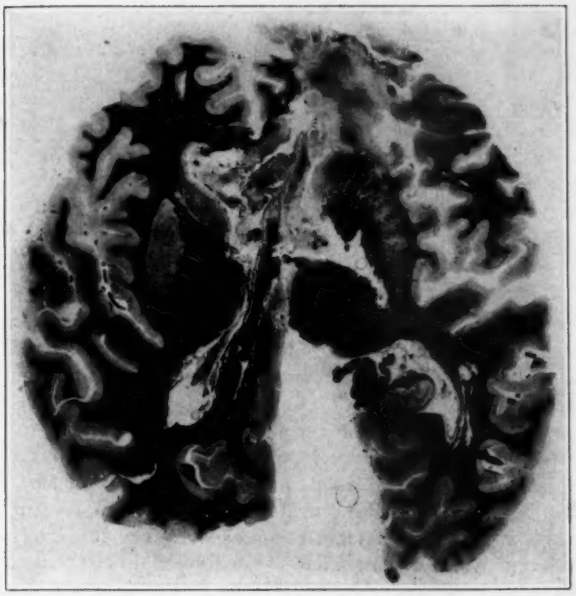

Fig. 11.—Demyelinization of the right frontal lobe, part of the corpus callosum and the anterior part of the right capsula externa. There is pus in both ventricles. Weigert stain; × ⅓.

Fig. 12.—Demyelinization of the white matter of the right parietal and temporal lobes, the right capsula interna and the anterior half of the corpus callosum. Weigert stain; × ½.

three years before admission to the hospital. Examination disclosed expressive aphasia, concentric contraction of the visual fields, with edema of the disks, but no measurable choking. There were central palsy of the right seventh nerve, right hemiparesis and some incoordination on the right. All tendon reflexes were equal and overactive. The dynamometric pressure was 90 mm. on the right and 145 mm. on the left. The pressure of the spinal fluid was 235 mm. of water, but the fluid was otherwise normal. Roentgen examination of the skull showed extrasellar erosion. Operation was performed, but the patient died a few days later.

Pathologic Observations.—Frontal section through the anterior part of the corpus callosum revealed advanced demyelinization of the white matter of the semioval center and the internal and external capsules on the right. The corpus callosum was greatly thickened, and there was a small area of demyelinization in the left gyrus cinguli (fig. 12). Section through the midpart of the thalamus disclosed a similar picture. On the right the semioval center, corona radiata, internal capsule and basal ganglia were demyelinated, and there was also demyelinization in the white matter of the insula and the right temporal lobe. The midpart of the corpus callosum was of normal width and myelin content. There was moderate demyelinization in the right occipital lobe. The tumor also invaded the midbrain (the corpora quadrigemina and the red nuclei), but the pons and medulla remained free.

Interpretation.—The severe involvement of the entire right hemisphere suggested that the nucleus of the tumor was in the semioval center in the right frontal lobe, from which it invaded the entire right hemisphere, the internal capsule and the brain stem. The involvement in this case demonstrates that invasion of the corpus callosum, even in far advanced unilateral astrocytoma, may occur very late, the opposite side consequently remaining free from tumor; at the same time, it illustrates an important feature of the unilateral variety—the invasion of the brain stem.

COMMENT AND SUMMARY

Astrocytoma of the cerebrum is a diffusely growing tumor which invades large areas of one or both hemispheres, and frequently also the brain stem. The growth starts in an area which is the nucleus of the tumor, from which the astrocytes regularly invade and destroy the myelinated tracts. This peculiarity of growth is the explanation of the characteristic infiltrative propensity of this neoplasm.

Astrocytomas of the hemispheres can be divided into bilateral and unilateral groups. Bilateral astrocytoma is frequent, the tumor in five of twelve cases described here belonging to this type. In this respect the astrocytoma differs greatly from other gliomas, in which bilateral involvement is rare. Bilateral invasion occurs when the nucleus of the tumor is in the corpus callosum. The location of the nucleus of the tumor in this structure determines the modus of the distribution. If the tumor arises in the genu of the corpus callosum the growth involves both frontal lobes and the anterior parts of both parietal lobes (case 2). In such cases invasion of the internal capsule may be limited, and the basal ganglia may be spared. A tumor arising in the anterior half of the body of the corpus callosum invades bilaterally the white matter

of the parietal lobe, the internal capsule, the basal ganglia and the brain stem (case 1), or it may involve the entire brain (case 3). A tumor arising in the splenium of the corpus callosum invades the temporal and occipital lobes and the basal ganglia bilaterally (case 5). If the nucleus of the tumor in the corpus callosum is very large or the tumor invades the entire corpus callosum at an early stage, universal invasion of the brain follows (case 4).

Unilateral astrocytomas can be divided into those involving the entire hemisphere and those involving a part of it. To the first group belongs the tumor in case 12; to the second, those in six cases: two in the parietal lobe, three in the temporal lobe and one in the frontal lobe. Such a subdivision is of practical value but is schematic, since astrocytoma always tends to invade the adjacent areas; thus, a tumor of the parietal lobe tends to invade the basal ganglia and the frontal and occipital lobes, and a tumor of the temporal lobe frequently invades the occipital region. The unilateral variety shows little tendency to invade the corpus callosum, even when the entire hemisphere is involved (case 12) or the nucleus of the tumor is near the corpus callosum (cases 6, 7 and 11). Limited invasion of the opposite hemisphere occurred in one case of astrocytoma of the temporal lobe, the invasion taking place through the fasciculus inferior thalami and the tuber cinereum. The most important property of the unilateral astrocytoma is the tendency to invade the pyramidal tracts and the brain stem (cases 8 and 12).

In some advanced stages the tumor may invade the perivascular spaces, resulting in irregular infiltration of the white and gray matter. This may occur in both the unilateral and the bilateral astrocytoma (cases 5, 7 and 9).

CHANGES IN THE BRAIN IN PLEXECTOMIZED DOGS

WITH COMMENTS ON THE CEREBROSPINAL FLUID *

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Much as facts furnished by neuropathologic observations speak against the hypothesis that the origin of the cerebrospinal fluid is largely, if not exclusively, in the choroid plexus, such a hypothesis is almost generally accepted and considered by some as dogma. This attitude is due largely to conclusions which Dandy [1] thought he was justified in drawing from his experiments with removal of the choroid plexus in animals (plexectomy). Dandy was so carried away by the interpretations of his experiments that he did not hesitate to aver [2] that experimental data are much more valuable than facts furnished by pathologic research and that the latter is a "dangerous method," for it "eventually has to satisfy a number of experiments which are more or less crucial." It would probably be more rational to claim the reverse —that "crucial" experiments should satisfy the facts furnished by human pathology and that it is not safe to form conclusions from experimental work of the sort that, for instance, he himself instituted and tried to interpret. Though it would seem not only unreasonable but incomprehensible to place a fundamental science like pathology beneath what is produced artificially in animals, statements such as the aforementioned make unfortunate impressions, especially on uncritical persons. The consequence is deplorable confusion, misunderstanding and a reactionary attitude toward facts that are obtained not only from pathologic but also from clinical observations. The current views as to the origin of the spinal fluid are so much at variance with those

* The responsibility of the junior authors in this work is limited to preparation of the experimental animals.

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1. Dandy, W.: Experimental Hydrocephalus, Tr. Am. S. A. **37**:397, 1919.
2. Dandy, W., in discussion on Hassin,[11a] p. 1185.

which are derived from clinicopathologic observations that it was thought advisable to repeat Dandy's experiments with a view to determining, if possible, the cause of the discrepancy. The experiments of Dandy have therefore been repeated on thirty dogs. The technic used in these experiments was the same as that used by Dandy, with slight modifications. The defect in the cortex caused by its incision was not sutured (Dandy,[1] page 406), and, instead of fascia or peritoneum, fascia and muscle were used to block the foramina of Monro.

The animals were allowed to live for from two days to eight months. As a rule, they were killed, as spontaneous death evidently does not occur from injuries caused by removal of the choroid plexus. From the start it was found that some phases of the experiments, such as blocking the sylvian aqueduct and complete removal of the choroid plexus, could not always be carried out as easily as one may judge from reading Dandy's report. In all our experiments, for instance, the pledget of cotton deviated slightly—as it did also in Dandy's experiments—from the course followed by the sylvian aqueduct and, as has been shown elsewhere,[3] exhibited a number of reactive manifestations that have nothing to do with the function of the choroid plexus. Yet Dandy labored under the erroneous impression that he had merely blocked the sylvian aqueduct. As his figures 2-b[1] and 8[c] show, the obstruction was not in the aqueduct, which is well pictured in figures 2-a[1] and 7, from which the previously mentioned photographs differ markedly. Attention is directed to this mishap not because it has any particular bearing on the problem of the alleged formation of spinal fluid by the choroid plexus but because it shows that artefacts may be caused by experiments and that, as they are assumed to be facts, they consequently may lead to improper conclusions.

In pathology only interpretation of the facts may be erroneous, but artefacts are not counted as facts. For this reason, conclusions derived from proper analysis of pathologic observations are safer than those from experiments and by no means "dangerous."

REPORT OF THE INVESTIGATION

I. *Attempts to Block the Sylvian Aqueduct.*—Blocking the sylvian aqueduct was attempted in fifteen dogs. Two of the animals died on the same day, and the brain of another was mutilated from a hemorrhage into the fourth ventricle and cerebellum. The rest of the animals lived, or were kept alive, for from five days to five months. In none of the animals was it possible to block the sylvian aqueduct. In the majority the plug was dislocated; in others it obliterated the fourth ventricle (fig. 1) instead of the third, without causing damage to the dog's health or life. In three of the twelve dogs the obstruction was placed in

3. Hassin, George B.: Reacting Cells in the Brain in the Presence of a Foreign Body, Arch. Neurol. & Psychiat. **36**:231 (Aug.) 1936.

the fourth ventricle; in the others it was pushed sidewise, as shown in the picture. In such animals hydrocephalus was present; that is, there were changes in the size of the lateral ventricles, as well of the third ventricle and the sylvian aqueduct, but only when the fourth ventricle was obstructed.

In general, experiments with blocking the sylvian aqueduct are superfluous, for plenty of instances of its obliteration are furnished by

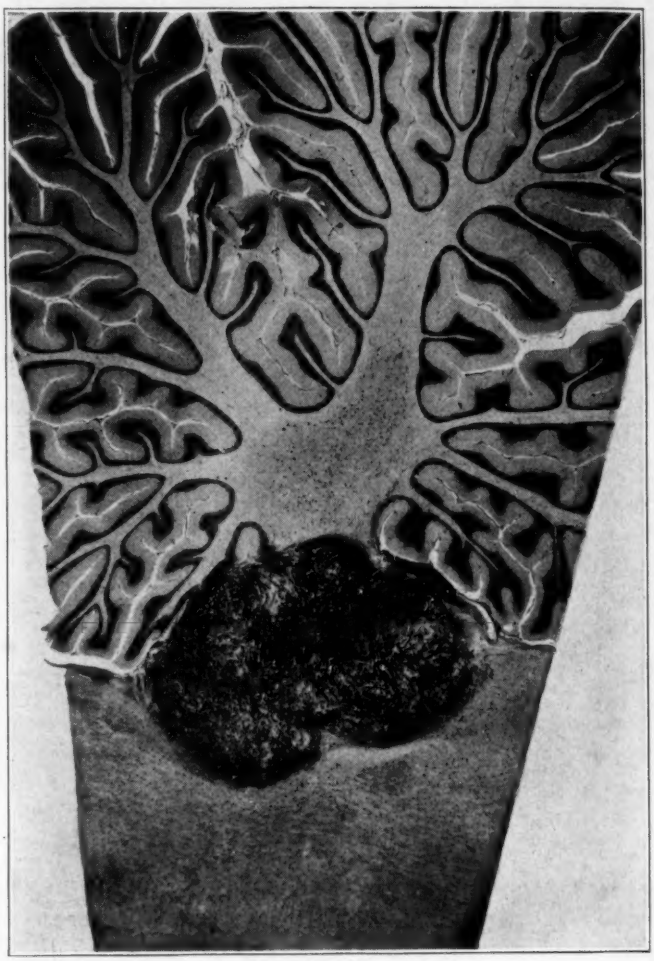

Fig. 1.—The fourth ventricle was plugged by a pledget of cotton. Toluidine blue stain.

human pathology (as the result of inflammatory conditions, tumor or congenital atresia). In such cases hydrocephalus results because the fluid content of the ventricles, whatever its origin, cannot be removed, as the avenue of escape is blocked. However, hydrocephalus resulting

from such obstructions, whether artificial or pathologic, may be caused not only by the almost generally assumed secretion of the choroid plexus within the ventricle but by the constant inflow of fluids from outside the ventricles—the cerebral tissues.

The tissue fluids in which the cerebral parenchyma is bathed are discharged in two directions—toward the cerebral ventricles and toward the subarachnoid spaces. In both instances drainage occurs by way of the Virchow-Robin spaces. In hydrocephalus the subarachnoid space is, like the ventricles, distended with fluid which, so to speak, cannot be accommodated by the ventricles, which are already overfilled. For this reason, it must be discharged in increased quantities into the subarachnoid space and thus contributes to its distention and the consequent formation of external hydrocephalus. The ability of the subarachnoid space to relieve the brain of the continuous addition of tissue fluids to the ventricles may explain the fact that hydrocephalus may exist for many years without endangering life. Roback and Gerstle,[4] for instance, stated that only a few of their patients with hydrocephalus caused by congenital atresia and stenosis of the aqueduct of Sylvius were infants in the first months of life and that a surprisingly large number were adults and older children. This would hardly be possible if the spinal fluid originated from the choroid plexus and was kept within the ventricles, for, since it would be unable to escape because its exits were blocked, so much would form that it would ultimately wreck the brain. On the other hand, if one assumes that the ventricular fluid does not come from the choroid plexus but represents the tissue fluids of the brain itself, discharged both into the ventricles and into the subarachnoid space, it is possible to conceive that when the ventricles and the pathways leading to them are overfilled or obstructed the other pathways, directed toward the subarachnoid space, are still comparatively free. The fluid then can flow to the subarachnoid space in larger amounts, thus relieving the enormous tension in the cerebral ventricles and the cerebral tissues themselves. At any rate, formation of hydrocephalus resulting from experimental or pathologic obstruction of the cerebral ventricular system does not prove that the cerebrospinal fluid is secreted by the choroid plexus.

Nor is it proved by the facts obtainable from experiments with removal of the choroid plexus from the lateral ventricles.

II. *Removal of the Choroid Plexus from One Lateral Ventricle After Closure of the Ipsilateral Foramen of Monro with a Piece of Fascia and Muscle.*—No obliteration or collapse of the plexectomized ventricle was obtained but, as figure 2 shows, some portions of both lateral ventricles were slightly dilated. On the

4. Roback, Harry N., and Gerstle, Mark L.: Congenital Atresia and Stenosis of the Aqueduct of Sylvius: An Anatomic Study of Six Cases, Arch. Neurol. & Psychiat. **36**:248 (Aug.) 1936.

side of operation, where blocking of the incision can be seen, the right lateral ventricle contains only particles of the choroid plexus (*Pl*) and, on the whole, is as narrow as the contralateral ventricle, which harbors a full sized choroid plexus (*Pl*). The ventricles and their plexuses are exhibited under a higher power lens in figure 3 *A* and *B*. In one animal the ventricle deprived of the choroid plexus appeared even larger. Still more striking was the bilateral dilatation of the ventricles in another dog. It should be pointed out that, regardless of the careful technic, it was not possible to remove the choroid plexus in its entirety, for, as has been stated, fragments could invariably be demonstrated within the ventricles. As a rule they lay isolated from their walls; they were minute or fairly large and could be seen with an ordinary magnifying lens. The stroma of

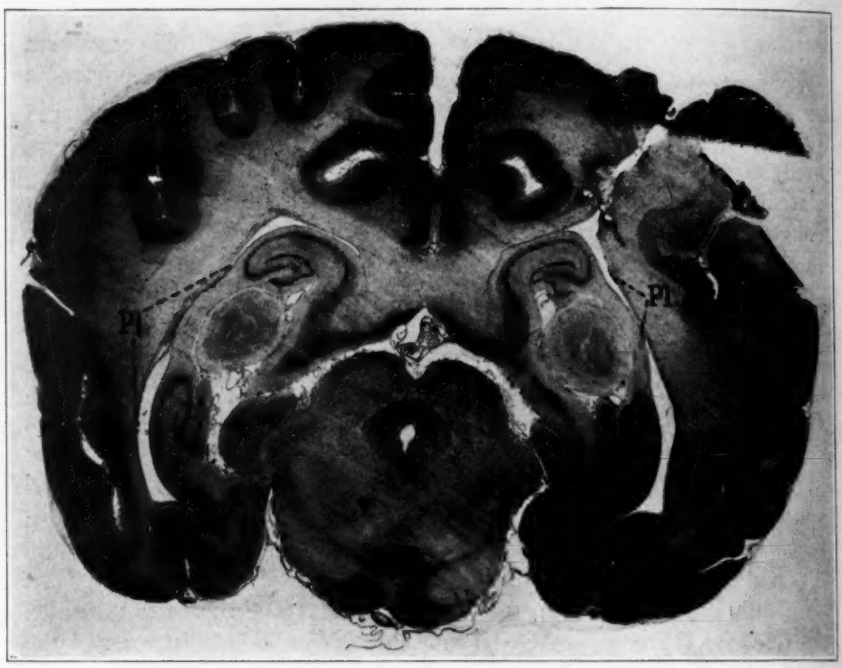

Fig. 2.—The right lateral ventricle was opened and the foramen of Monro blocked. Only particles of the choroid plexus can be seen in the right ventricle (*Pl*); yet this ventricle is of the same size as the left, where the choroid plexus (*Pl*) was not attacked. Both are reproduced under higher magnification in figure 3 *A* and *B*. Van Gieson stain; pyroxylin section.

such isolated tufts was always proliferated, enveloping the congested blood vessels as though strangulating them; the cells appeared vacuolated, the cytoplasm homogeneous and the nuclei pyknotic.

It may be assumed that the effect on the ventricular fluid contents of a broken-up plexus is equivalent to that of its complete removal, and, withal, it is questionable whether a choroid plexus torn and broken into small fragments, as in the cases just described, is capable of pro-

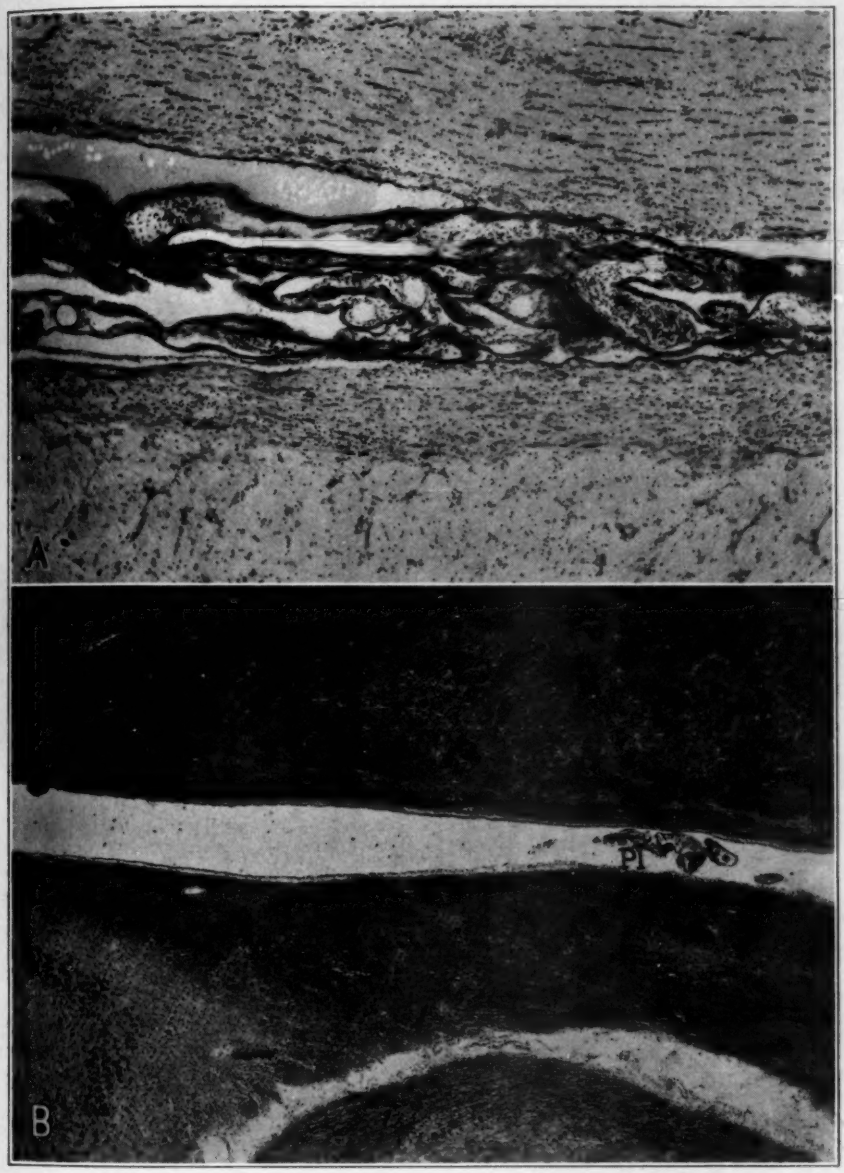

Fig. 3.—Photomicrographs with higher magnification (Van Gieson stain) of the brain shown in figure 2. *A* shows the undamaged choroid plexus of the left lateral ventricle, and *B*, remnants of the choroid plexus of the right lateral ventricle.

ducing spinal fluid. If it is, the secretion must be in much smaller quantities than normal and, accordingly, must result in the smaller size of the corresponding ventricles. This appears to be the case in figure 4 *A*, representing an unstained section of the brain of the dog, a stained section of which (from a different level) is pictured in figure 4 *B*. The

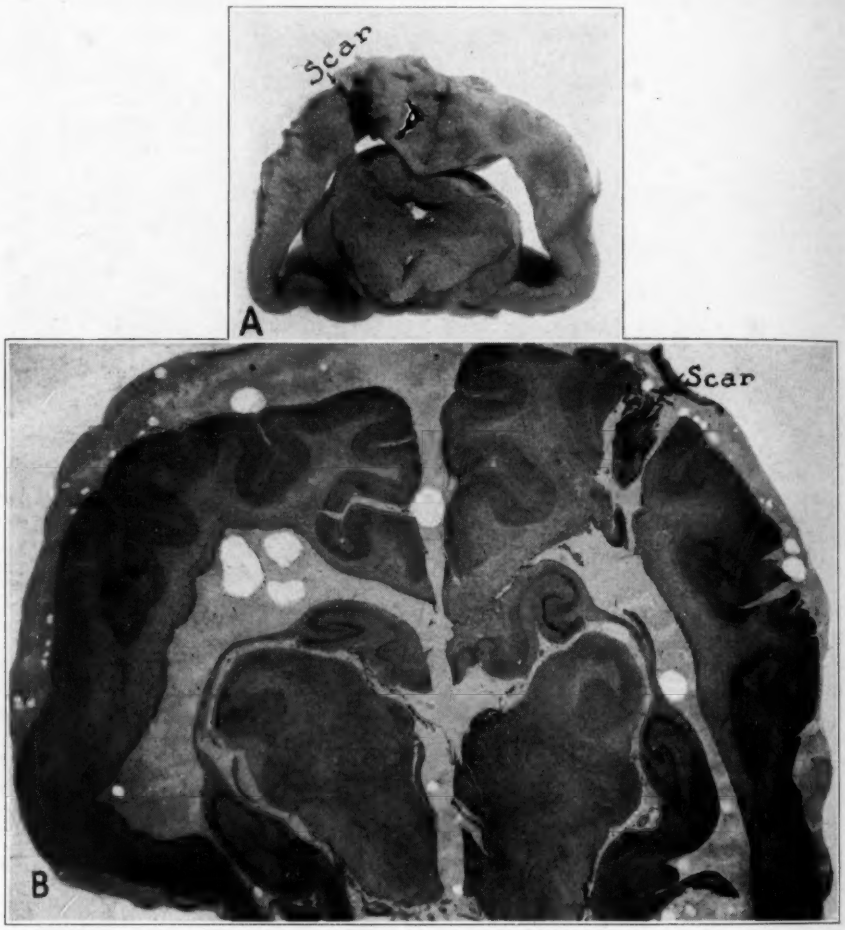

Fig. 4.—*A* shows the brain in the same case as that pictured in figure 4 *B*. The right ventricle (at the left of the picture) appears much more collapsed than that in *B*, but the collapse is due to asymmetry of the halves of the brain and to the scar. *B* (toluidine blue stain) shows that both ventricles are dilated, though only the right choroid plexus had been removed. The inequality in the size of the ventricles is artificial and is due to asymmetry of the halves of the brain.

second section shows a collapsed ventricle from which the plexus has been removed, but the collapse, when compared with that in figure 4 *A*,

proved not to be real. It was due partly to collapse of the opposite half of the brain and partly to shrinkage brought on by the formation of a large scar in the ipsilateral cortex. By restoring the collapsed half to a normal position it was possible to show that the collapsed ventricle on the side of operation was of as great size as that on the opposite, healthy side, and by no means smaller. The scar is probably an additional factor which may affect the size of the ventricle, and possibly also its contents. The incisions in the cortex and subcortex through which the choroid plexus had been removed, extensive as they may have been, always became rapidly occluded by strands of connective tissue, which also obliterated the subdural and subarachnoid spaces

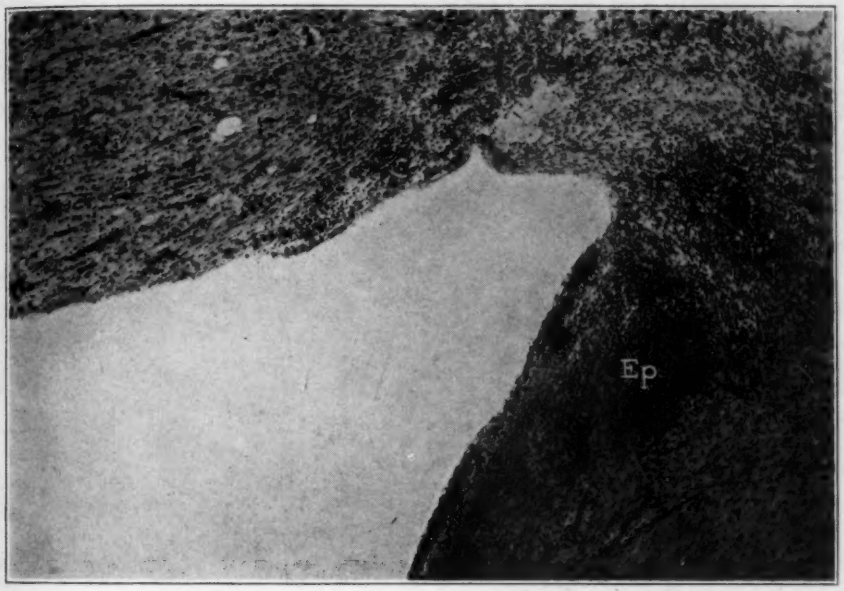

Fig. 5.—Ependyma and subependyma of the plexectomized lateral ventricle. The reactive phenomena are marked, especially in the area *Ep*.

(figs. 2 and 4 *B*). The strands, outgrowths of the cerebral meninges, invade the parenchyma and transform it into a large connective tissue scar. As figures 2 and 4 *A* and *B* show, the scar resembles a cork, a section of which revealed wedge-shaped infiltration (with lymphocytes, fibroblasts and polyblasts) of the hemisphere, extending down to the ventricle. The infiltrated area is divided from the healthy parenchyma by a degenerated area rich in gitter cells, lymphocytes and polyblasts.

The ventricular ependyma also showed marked changes (fig. 5). In some instances it was not pathologic; often it was hyperplastic and was represented by several layers of lining cells. In some cases the ependymal lining was devoid of cells and appeared to be desquamated

and separated from the subependymal tissues by a hemorrhagic layer. Other ependymal areas were covered with thin layers of blood or were ballooned and poor in cells. The ependymal cells themselves appeared densely stained, and their nuclei were pyknotic. The changes described extended from the meninges to the ependymal lining of the ventricles and, with the large scar, were at least partly responsible for the decreased size of the ventricle.

III. *Blocking of a Foramen of Monro Without Removal of the Choroid Plexus.*—Blocking a foramen of Monro was carried out in three dogs, in one of which one foramen was not blocked but only scarified. In this dog slight enlarge-

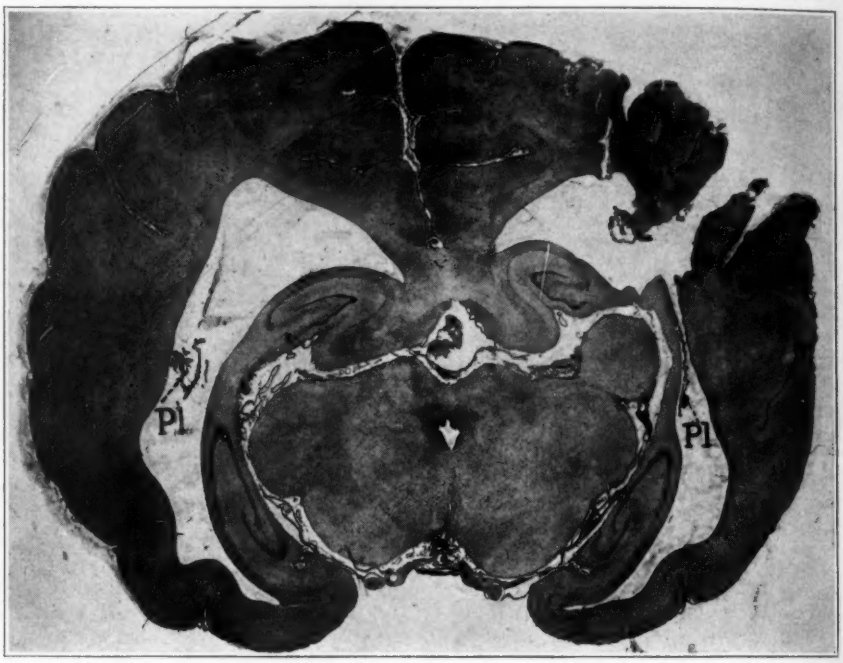

Fig. 6.—The right foramen of Monro was plugged, and the choroid plexus (on the right) was not removed, yet the size of the plugged ventricle is smaller than that of the left. The choroid plexus is present in both ventricles. The halves of the brain are slightly asymmetrical.

ment of the ventricle occurred on the side opposite that of operation. One would expect the reverse, as the reaction produced by this procedure in the ependyma and subependyma was not unlike that in the cases in which the foramen had been plugged. Whether the damage to the cortex and subcortex or the operative procedure itself affected the ventricle is not possible to tell.

In another dog the right foramen of Monro was plugged. The result was enlargement of the ventricle, not on the side of operation but on the contralateral side. In the third dog, which lived three months (fig. 6), bilateral hydrocephalus occurred. Probably because of the slight asymmetry of the halves of the brain, the right ventricle appeared slightly smaller.

Like hydrocephalus of the lateral ventricles produced by an artificial or a pathologic obstruction of the sylvian aqueduct or the third or fourth ventricle, hydrocephalus following obstruction of a foramen of Monro merely shows that the fluid cannot escape from the ventricles, whatever its source—the choroid plexus or tapping the cerebral tissue fluids. Experiments like those on the sylvian aqueduct cannot, and do not, prove that the cerebrospinal fluid is secreted by the choroid plexus.

IV. *Removal of Both Choroid Plexuses After Blocking Both Foramina of Monro.*—The animals were kept alive from three to three and one-half months. The ventricles did not show reduction in volume, as one might expect because of destruction of the larger portions of the choroid plexus. Of the histologic changes, aside from those outlined previously, thickening of the ependyma was especially in evidence. This was well seen in the dog in which dilatation instead of collapse of the ventricle was present.

This observation speaks strongly in favor of the assumption that the cerebrospinal fluid originates not in the choroid plexus but elsewhere.

COMMENT

Of the types of experiments described here, that described under heading IV seems decisive. Such experiments are worth repeating, which should be easy with the abundance of neurosurgical talent in the United States. It would seem that were the choroid plexuses the source of the cerebrospinal fluid, their excision should result in dry and collapsed ventricles, which, as has been shown, is not the case. One should also consider the structural changes occurring in plexectomized brains. Such changes were observed in the meninges, the parenchyma and the ependymal lining and represented reactions of the aforementioned tissues to the incision and the presence of a foreign body which was used as a plug. Microscopic observations also revealed the presence of small fragments of choroid plexus in the ventricles from which total removal of the plexus was attempted. As has been indicated, such a plexus reduced to minute fragments is hardly capable of producing fluid. It is a plexus without a function, and in its effect on the size of the ventricles or the amount of ventricular fluid it is supposed to produce, it should be considered equivalent to the condition that results from complete plexectomy.

The morphologic changes mentioned are by no means meaningless. They should be borne in mind in evaluating the results of the experiments, as they may suggest entirely different interpretations of the observations and arouse doubts as to whether the experiments are "crucial." For instance, the large scar caused by the inserted plug must, as has been indicated, affect by shrinking the size of the ipsilateral ventricle; the ependymal changes, which were promiscuous in every case, must have an effect on the condition of the ventricular contents.

Thus, in Arnold's [5] cases typical ependymal granulations, probably of inflammatory origin, extended into the foramina of Monro and, with the "swollen" choroid plexus, caused their obstruction and hydrocephalus of the lateral ventricles. In Spiller's [6] cases similar ependymal changes around one foramen of Monro produced unilateral hydrocephalus. The individual rôles of the ependyma and the "swollen" choroid plexus in Arnold's case cannot be clearly determined, but Arnold emphasized that the principal cause of the obstruction of the foramen of Monro was the lesion of the ependyma and subependyma, along with that of the choroid plexus.

Clearer and more significant are the facts furnished by removal of the choroid plexus in human beings. Such an operation is performed for the purpose of relieving the accumulation of cerebrospinal fluid, on the assumption that the fluid is produced by the choroid plexus and that removal of the plexus will consequently prevent its further formation and thus reduce the already existing hydrocephalus.

Dr. Tracy Putnam, of Boston; Dr. James R. Jaeger, of Denver, and Dr. Harold C. Voris, of Chicago, have furnished us with valuable material. Dr. Putnam's patients had all been operated on by a specially constructed electric rod, called by him a coagulating ventriculoscope. By this method Putnam destroyed the choroid plexus "bit by bit" in from five to twenty minutes. One choroid was coagulated at one time. Some patients survived the operation as long as seventeen weeks, and diminution of the circumference of the head (in one case, from 73 to 67 cm.) could be noticed after the operation. Pathologic studies of five brains (only remnants of one were delivered to us) revealed: reduction of the hemispheres to thin, almost transparent, membranes and remnants of the choroid plexus in the lateral ventricles. In the fragmented brain, however, the plexus was observed only in the fourth ventricle, and in another brain, in the third ventricle. In addition, there were marked external hydrocephalus, ependymal changes (ependymitis, subependymitis and desquamation of the ependyma), rarefaction of the cerebral parenchyma and changes in the tuft cells. Accidental changes were aseptic meningitis and evidences of surgical intervention, such as hemorrhages. In short, the changes were similar to those observed in the experimental animals, but more marked. The most noteworthy facts were: presence of remnants of the choroid plexus, which (as in our experimental cases) evidently could not be removed, in spite of the refined and ingenious technic used; persistent hydrocephalus,

5. Arnold, J. G.: Primary Ependymitis: Subacute Type with Occlusion of the Foramina of Monro and Hydrocephalus of the Lateral Ventricles, Arch. Neurol. & Psychiat. **32**:143 (July) 1934.

6. Spiller, W.: Two Cases of Partial Internal Hydrocephalus from Closure of the Interventricular Passages, Am. J. M. Sc. **124**:44 (July) 1902.

regardless of removal of the major portion of the choroid plexus, and the manifest uselessness of the surgical procedure. The reduction in the size of the head emphasized by Putnam [7] in some of his cases may be attributed to factors which have already been mentioned and which may be gathered from the cases of Jaeger.[8]

Jaeger operated on an infant aged 6 weeks with "the intention of opening the floor of the third ventricle into the basal cistern." When he opened the skull in the lower part of the temporal region and incised the dura, he "came down on a thin membrane," not more than 1 mm. thick, which was the remnant of the cerebral cortex. Enough fluid was evacuated from the ventricle to obtain a good look into the interior of the brain, and he could see that the whole brain on the side which had been opened apparently was represented only by a thin membranous sac and that there was "no point in proceeding with the operation." The wound was closed with silk sutures, and there was healing without incident. The head rapidly began to shrink, and soon the fontanels were markedly depressed, so that the bony framework of the skull stood out in marked relief. Death occurred three weeks after operation, apparently from too rapid loss of fluid from the inside of the skull. Necropsy showed: stricture of the sylvian aqueduct, which had been the diagnosis at operation; normal brain tissue at the tips of the frontal and occipital lobes; a thin membrane replacing the intervening brain structure, as described at operation; the huge size of the ventricular cavities and a normal brain stem and cerebellum. On gross inspection, the lining of the ventricles appeared to be inflamed. The choroid plexus was hemorrhagic but present; the cortex had for the most part disappeared and was represented in many areas by the ependymal lining, which generally was thickened.

Jaeger justly emphasized that, as no plexectomy had been performed on this patient, the silk sutures which were applied to the wound "evidently caused the head to collapse." Probably the action of the sutures was similar to that of the scar in the brain of one of our dogs (in the experiments described under heading III). Jaeger also considered the possibility of ependymal changes, which he thought were probably caused by the bloody ventricular fluid, which in some way affected the ependyma and indirectly had something to do with the volume of fluid in the ventricles. Whatever rôle the ependyma may play, one must agree with Jaeger that removal of the choroid plexus is not the factor that causes decrease in hydrocephalus, that other factors are at play and that after operation on a hydrocephalic brain the head frequently decreases in size "at a very rapid rate."

Even more interesting is Jaeger's observation on another infant, aged 5½ weeks, with congenital hydrocephalus, on whom plexectomy had been performed, with the removal of 250 cc. of fluid. The choroid plexus was of normal size. The fluid accumulated as early as three days after operation, in spite of daily removals of from 10 to 20 cc. of spinal fluid. One month later plexectomy was performed

7. Putnam, Tracy: Personal communications to the senior author.
8. Jaeger, J. R.: Personal communications to the senior author.

on the other side and, again, a normal choroid plexus was observed. Ten days later, just before the patient's death, the head measured 1 inch (2.54 cm.) less. Histologic studies in our laboratory revealed: nonsuppurative meningitis; thinning of the cortex, especially of the occipital lobes; a patent sylvian aqueduct, and thickened ependyma throughout the ventricular system, including the aqueduct and the fourth ventricle, where the ependymal cells were not desquamated. In the lateral ventricles the cells were elongated, hypertrophied and covered by a mass of amorphous substance. The base of the brain was covered by a thickened pia-arachnoid; the white cerebral substance was rarefied, and a tiny strand of the choroid plexus was present over the optic thalamus.

The interest in this case was the "slow diminution, if any," of the amount of the fluid, in spite of the practical absence of the choroid plexus and the severe ependymal and subependymal changes.

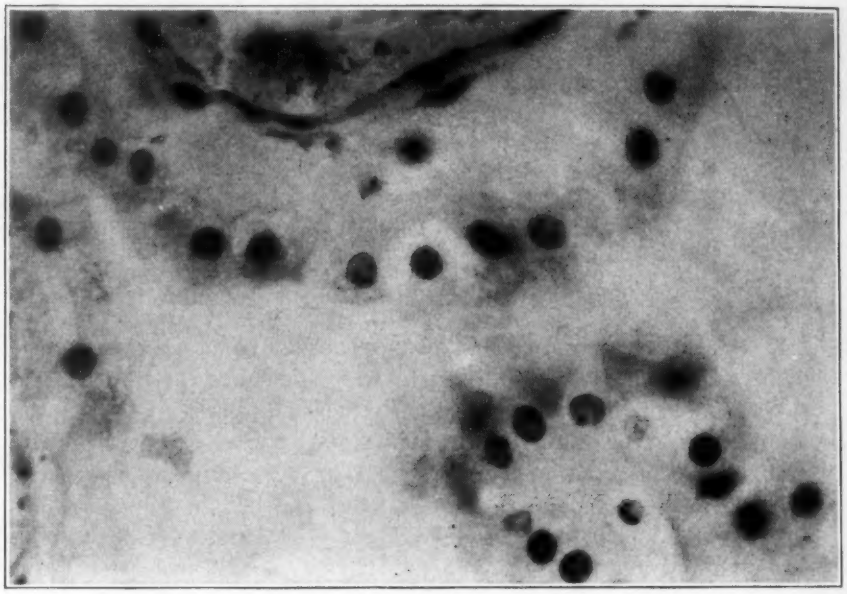

Fig. 7.—Choroid plexus removed from a hydrocephalic child at operation. The tuft cells are large and colorless. Some are reproduced in the drawing in figure 8. Hematoxylin and eosin stain; × 1,000.

The tuft cells of the well preserved choroid plexus in hydrocephalus are usually not pathologic. However, the choroid plexus is seldom entirely preserved in hydrocephalus; when it is the tuft cells are decidedly pathologic. Figures 7 and 8 present such changes in the cells of the choroid plexus of an infant aged 3 months, on whom Dr. Voris [9] operated.

The infant was born prematurely at 8 months. There was hydrocephalus, with flexor contraction spasm and no tonic cervical reflexes. When the head was

9. Voris, Harold C.: Personal communications to the senior author.

opened, there was no gross evidence of the cerebral hemispheres; the brain stem with the optic thalami and the third ventricle were present, and the basal ganglia were open. There were no traces of choroid plexus in the lateral ventricles. Two buds of the choroid plexus were floating freely in the cavity and were attached to the anterior end of the third ventricle. Histologic examination of one of the buds showed disrupted, vacuolated tuft cells (figs. 7 and 8); some were of large size, and others were small and packed, especially the smaller ones, with numerous dark granules, the nature of which could not be determined. Some cells showed only a framework of trabeculae, which were also granular, and were often without contents except a densely stained nucleus in the lower third of the cell body; in some cells there were two nuclei. The basal membrane was lacking, and the stroma showed, aside from hemorrhages, immense infiltrations with lymphocytes and polyblasts. The blood vessels, which were enormously dilated, were occasionally filled with a homogeneous mass, which was also present in the stroma.

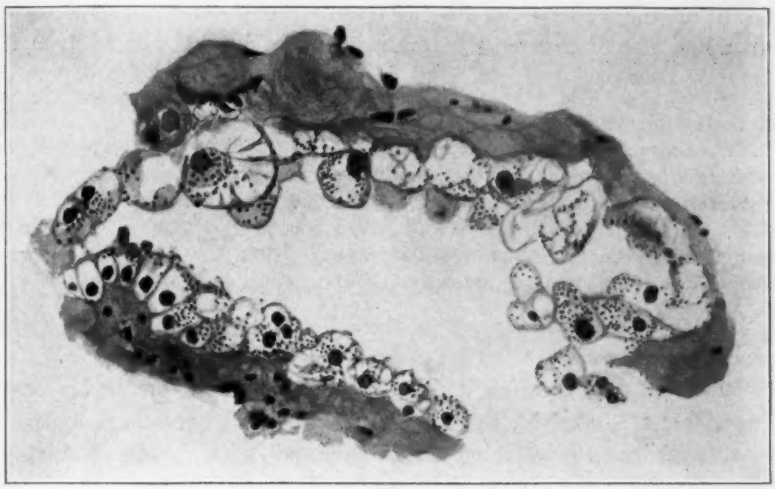

Fig. 8.—Some of the tuft cells shown in figure 7. The explanation appears in the text.

These are the facts obtained from plexectomized human beings. Dogs were plexectomized to demonstrate lack of formation of cerebrospinal fluid; human beings were and are plexectomized to obtain reduction in the volume of ventricular fluid, excessively formed. Neither the experimental nor the pathologic group furnished conclusive evidence that the choroid plexus produces cerebrospinal fluid. The evidence furnished by pathologic studies of the plexectomized human beings is certainly more conclusive than that to be derived from the plexectomized dogs. The amount of cerebrospinal fluid did not decrease appreciably; if it did occasionally, it was probably not due to plexectomy. While arguments for or against such a view may not appear convincing, the cases, like that of Voris, in which only two small,

floating buds of choroid plexus were observed in the presence of enormous hydrocephalus, should be convincing and of greater value than all the "crucial" experiments combined. None would accuse the small buds of working overtime to produce spinal fluid, as the few cells they possessed were disrupted and practically functionless. Unfortunately, the fable that the choroid plexus is the source of spinal fluid has obtained such a firm hold on the large majority of investigators and clinicians that the significance of such an important fact as a sclerosed choroid plexus is entirely ignored. As an illustration, the case of unilateral hydrocephalus described by Dott [10] may be cited. In his patient, a child aged 9 months, the hydrocephalus was due to obstruction of one foramen of Monro for approximately four months. The cause was probably inflammation of the ventricular walls, which, as seen at operation, were lined by a layer of organized fibrous scar tissue, which had also obliterated the foramen of Monro. At operation Dott [10] observed that

> the choroid plexus [was] buried in the organized tissue which lined the ventricle . . . as a purplish streak, but the ventricular surface over it was quite smooth. Its excision was . . . out of the question. The appearance suggested that it must be practically functionless. . . . [The fluid in the ventricle was brownish.] . . . A part of the normal choroid plexus was . . . floating freely in the clear fluid. When the cavity was dried out, drops of clear fluid could be seen exuding from the surface of the actively secreting plexus.

Whatever the meaning of the so-called sweating, or actively secreting, choroid plexus, Dott did not hesitate to emphasize its occurrence but did not consider it necessary even to hint that in his case a "functionless," "buried" choroid plexus produced hydrocephalus which he successfully relieved by creating a communication through the septum pellucidum with the contralateral ventricle.

Cases like those of Dott and Voris are by no means rare and have been referred to elsewhere.[11] It is obvious that if a sclerosed choroid plexus cannot prevent increase in hydrocephalus, the surgical removal of the plexus can serve no purpose whatever. Even if the plexus could be removed completely from the lateral ventricles, it could not be removed from the third ventricle, where it is also supposed to produce cerebrospinal fluid. Even Dandy realized the futility of such a procedure because of danger of fatal hemorrhage. Plexectomy has

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10. Dott, N. M.: A Case of Left Unilateral Hydrocephalus in an Infant; Operation; Cure, Brain **50**:548, 1927.

11. Hassin, George B.: (*a*) Hydrocephalus: Studies of the Pathology and Pathogenesis, with Remarks on the Cerebrospinal Fluid, Arch. Neurol. & Psychiat. **24**:1164 (Dec.) 1930; (*b*) Hydrocephalus: Report of a Case in an Infant with Vestiges of a Choroid Plexus in the Fourth Ventricle Only, ibid. **27**:406 (Feb.) 1932.

thus no rational basis, for the choroid plexus is an organ not of secretion of spinal fluid but of excretion. It removes from the ventricular fluid various substances and renders it absorbable. This has repeatedly been discussed elsewhere.[12]

CONCLUSIONS

1. Plexectomized brains exhibit structural changes: scar formation; reactive inflammatory phenomena (lymphocytic and polyblastic infiltrations of the incised tissues, ependymitis and subependymitis), and degenerative changes with the formation of fat granule bodies.

2. In hydrocephalus occurring in man the choroid plexus may be reduced to mere remnants—a strand of fibrous connective tissue—and the remaining tuft cells may undergo granular breaking up, yet the further growth of hydrocephalus is not affected, even when the corresponding foramen of Monro is blocked.

3. Experimental plexectomy does not give uniform results—the plexectomized ventricle may be smaller than the normal ventricle, of the same size or even larger. The size may be affected by large scars that result from operative procedures.

4. Both pathologic and experimental data indicate that cerebrospinal fluid forms in the ventricles, but not from the choroid plexus. It comes only from the cerebral tissue fluids drained by the ventricles (through the connecting Virchow-Robin channels).

5. The presence of external hydrocephalus denotes the existence of an additional draining system (in the subarachnoid space), which is of the same anatomicoclinical significance as internal hydrocephalus.

6. Pathologic observations on hydrocephalus in man, whether made during operation or at necropsy, are more reliable than experimental observations which, like plexectomy in human beings, are on the whole misleading, unnecessary and unconvincing.

7. The only experiments of value in connection with plexectomy would be the creation of conditions resembling those outlined in the second conclusion, i. e., removal of the choroid plexus from one or both ventricles after preliminary blocking of the corresponding foramen of Monro, thus isolating the lateral ventricles from the third ventricle and its choroid plexus. The other types of experiments are superfluous, as they do not prove that the cerebrospinal fluid is formed by the choroid plexus.

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12. Hassin, George B.: Histopathology of the Peripheral and Central Nervous System, Baltimore, William Wood & Company, 1933, p. 359.

ENOSTOSES WITHIN THE CALVARIUM

SURVEY OF SKULLS IN THE WARREN MUSEUM OF THE HARVARD UNIVERSITY MEDICAL SCHOOL

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Among the many treasures in the Warren Museum of the Harvard University Medical School is a collection of about 1,000 skulls (complete or incomplete). If one excludes those which are fastened to the bony skeleton or to the vertebrae by their ligaments and the skulls of children, there are about 800. These may be divided into two groups, the first representing chiefly donations of about 300 skulls from various sources and the second a formal group of 500 skulls of prehistoric Peruvian Indians.

Of the first group, many of the skulls came to the Warren family through personal friends in the early years, from 1783, when their historical collection was begun, and almost all the donations were made several years before 1847, when the Warren Museum was given to the medical school and established there. The names of R. M. Hodges, O. W. Holmes, George C. Shattuck, J. J. Astor, W. T. G. Morton and H. J. Bigelow occur in the museum catalog as donors, as well as that of Captain Isaac Hull, U.S.N., for whom a street in Boston is named. One can visualize hearty Captain Hull, in dress uniform, dining at the Warren household and reciting anecdotes and the steps taken to locate and obtain this or that specimen in ports on the west coast of South America. He had many commands after the battle in which his ship, the "Constitution," was victorious; one of them was standing by outside the port of Lima, Peru, for three years.

In the Civil War period of the 1860's, many skulls of North American Indians were garnered from various sources—from Damariscotta, Maine, and Milton and Sudbury, Mass., to as far west as the Columbia River and as far south as Georgia. Other personal donations from traveling friends continued throughout the following years.

Whenever pathologic skulls were observed in the anatomic dissecting-room of the medical school, they, too, were added to the collection. Occasionally one finds that a purchase was made and recorded in the museum catalog. Altogether, in this group about 300 skulls were available for examination. Some of the skulls were intact and had to be examined by inserting a clinical flash-light through the foramen magnum. From the front of the skull the transmission of light could

be judged; by peering with the light from the base, the condition of the inner table, the pressure thinnings for the pacchionian bodies near the midline and the state of the sutures could all be ascertained. When the specimens were of the calvarium only, they could be viewed directly and the condition of the inner table immediately determined. Besides the skulls of North American Indians (45), Peruvians (19) and Hindus (19), there were those of Egyptians, Africans, Romans, Abyssinians, Chinese, Greeks, Sandwich Islanders, Madagascans, Eskimos, Cossacks and Mexicans; for others the racial identity was not specified. No trace of a pathologic bony deposit was seen on the inner table of any bone in skulls of any of the known races! A summary of observations follows.

Total number of skulls and calvaria examined in group 1	300
Skulls with general thickening	7
Skulls with thickening of the frontal or parietal bones	8
Skulls with enostoses of the frontal bone	10

The second group is the Tello collection of skulls of prehistoric Peruvian Indians, purchased by Dr. Charles G. Weld in 1911 as a special gift to Dr. William Fiske Whitney, the second curator of the museum from 1879 to 1921. This collection numbers in all about 600 skulls, some of which are still attached to the skeleton and others have adherent membranes or an occluded foramen magnum. Only 500 specimens were examined. In this group, as well as in the skulls of racial groups previously named, no roughening of any degree was seen on the inner table.

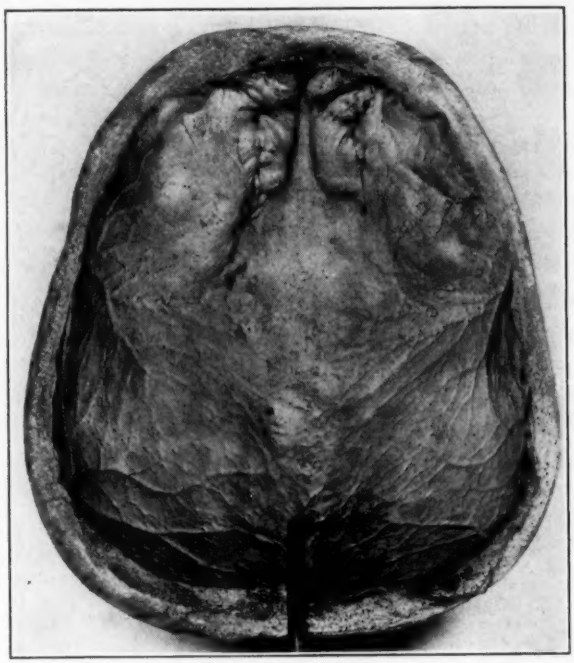
Many of these skulls in the second group have been trephined—some more than once—and some of the openings remain, though in others there is evidence of repair near the periphery; in a few the entire opening has been filled in by bone.

COMMENT

For association with the presence of enostoses, there is no record of age, sex or illness for many of the skulls. In the collection comprising the first group are 12 skulls marked syphilitic; examination showed that 2 of these had slight frontal roughening, so syphilis could not be charged with this change in the inner table. In the majority of specimens for which a diagnosis of syphilis was made, the disease showed its presence more markedly in the outer table. That syphilis was present in skulls of the second group, those of prehistoric Peruvian Indians, there is no indication grossly, and Hrdlička,[1] in his report on skeletons of Peruvian

1. Hrdlička, Aleš: Anthropological Work in Peru in 1913, with Notes on the Pathology of the Ancient Peruvians, Smithsonian Misc. Collect. (no. 18) **61**:1-69, 1914.

Indians, mentioned that he found any diagnostic traces of rachitis, osteomalacia, syphilis, tuberculosis or cancer to be absent and fractures to be few. In a series of 262 skulls of adults or near adults, he found one "osteoma on frontal, small." I assume that this was on the outside, since he made no mention of examining the inner aspect of the skulls.



Calvarium (no. 10,105; the Warren Museum), showing general thickening of the bones, no visible sutures, groovings for branches of the meningeal arteries and massive ingrowths, or enostoses, of the inner table.

SUMMARY

1. Dried specimens of 800 skulls were reviewed for the presence of enostoses on the inner table.

2. In the first group skulls of the races named showed no enostoses.

3. In the second group of skulls of prehistoric Peruvian Indians, numbering 500, no pathologic thickenings were found.

4. Did these prehistoric skulls antedate syphilis?

5. Are the skulls of primitive races exempt from enostoses?

6. In a few skulls (10), donated because of pathologic conditions, enostoses were observed (figure).

ARTERIAL SUPPLY OF LATERAL PAROLIVARY AREA OF THE MEDULLA OBLONGATA IN MAN

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Lesions of the lateral parolivary area of the medulla oblongata, such as occur in the syndromes described by Avellis,[1] Wallenberg,[2] Babinski and Nageotte[3] and Cestan and Chenais,[4] were after Wallenberg's[5] work generally regarded as due to occlusion of the posterior inferior cerebellar artery. Breuer and Marburg,[6] however, pointed out that similar lesions may be produced by thrombosis of the vertebral artery distal to the point of origin of the posterior inferior cerebellar artery or by that of the basilar artery, a fact which was confirmed by the extensive studies of Stopford.[7] In 1925 Foix, Hillemand and Schalit[8] described a new artery, the arteria fossae lateralis bulbi, and brought

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1. Avellis, G.: Klinische Beiträge zur halbseitigen Kehlkopflähmung, Berl. Klin. **40**:1, 1891.

2. Wallenberg, A.: Akute Bulbäraffektion (Embolie der Art. cerebelli post. inf. sin.), Arch. f. Psychiat. **23**:504, 1895.

3. Babinski, J., and Nageotte: Hémiasynergie, latéropulsion et myosis bulbaire avec hémianéstésie et hémiplégie croissées, Nouv. iconog. de la Salpêtrière **15**: 492, 1902.

4. Cestan, R., and Chenais, L.: Du myosis dans certaines lésions bulbaires en foyer (hémiplégie du type Avellis associée au syndrome oculaire sympathique), Gaz. d. hôp. **76**:1229, 1903.

5. Wallenberg, A.: Anatomischer Befund in einem als akute Bulbäraffektion (Embolie der Art. cerebelli inf. post. sin.?) beschriebenen Fall, Arch. f. Psychiat. **34**:923, 1901; Verschluss der Arteria cerebelli inferior posterior dextra (mit Sektionsbefund), Deutsche Ztschr. f. Nervenh. **73**:189, 1922.

6. Breuer, R., and Marburg, O.: Zur Klinik und Pathologie der apoplektiformen Bulbärparalyse, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **9**:181, 1902. Marburg, O.: Ueber die neueren Fortschritte in der topischen Diagnostik des Pons und der Oblongata, Deutsche Ztschr. f. Nervenh. **41**:41, 1911.

7. Stopford, J. S. B.: The Arteries of the Pons and Medulla Oblongata, J. Anat. & Physiol. **50**:131 and 255, 1916; **51**:250, 1917.

8. Foix, C.; Hillemand, P., and Schalit, I.: Sur le syndrome latéral du bulbe et l'irrigation du bulbe supérieur: L'artère de la fossette latérale du bulbe, le syndrome dit de la cérébelleuse inférieure, territoire de ces artères, Rev. neurol. **32**:160, 1925. Foix, C., and Hillemand, P.: Les artères de l'axe encéphalique jusqu'au diencéphale inclusivement, ibid. **32**:705, 1925.

substantial evidence to demonstrate that most lesions of the lateral parolivary area (Ziehen[9]), including part of the dorsal lamella of the inferior olive and the descending root of the trigeminus nerve and its nucleus, are caused by lesions of this artery. Merritt and Finland[10] confirmed their observations in a clinical and pathologic study.

After the early work of Adamkiewicz[11] and Duret,[12] the distribution of the larger arteries of the hindbrain within the medulla oblongata and the pons was thoroughly studied by means of injection methods by Stopford.[7] The smaller arteries, however, especially that described by Foix and his co-workers,[8] have not been studied by separate injection. In view of the recently emphasized clinical significance of these small arteries, we thought it advisable to undertake such a study.

MATERIAL AND METHODS

This study is based on twelve brains obtained at autopsy from presumably normal persons. The vascular distribution of the arteries of the pons, cerebellum and medulla oblongata was studied immediately after removal of the brain, and a diagram was made in each case. Subsequently one, and in some instances two, of these arteries were injected separately—in cases in which two arteries were injected contrasting material was used. Usually black was used for the anterior artery of the lateral parolivary fossa or for the anterior inferior cerebellar artery with its ramifications. The posterior inferior cerebellar artery with its ramifications was injected with red material. As black material for injection a dispersion of one part of india ink in 3 parts of a dilute solution of formaldehyde U. S. P. (1:10) was used and as red material, a similar dispersion of carmine or neutral red. The amount of injected material varied from 1 to 10 cc.; for the anterior artery of the lateral parolivary fossa usually from 1 to 3 cc. was used. After this procedure another diagram of the gross appearance of the injected vessels was made, and the material was hardened in a dilute solution of formaldehyde U. S. P. (1:10). Thick frozen sections of the medulla oblongata (from 200 to 400 microns) were cut in series. They were dehydrated and mounted as usual.

RESULTS

(A) Gross Anatomic Distribution of Arterial Blood Vessels on Surface of the Lateral Parolivary Fossa of the Medulla.—The arterial net on the surface of the lateral parolivary fossa is supplied by the following branches: (1) the anterior artery of the lateral parolivary fossa; (2) one or two arteriae intermediae of the lateral parolivary fossa and (3) the posterior artery of the lateral parolivary fossa. This

9. Ziehen, T.: Anatomie des Zentralnervensystems, Jena, Gustav Fischer, 1913, pt. 1.

10. Merritt, H. H., and Finland, M.: Vascular Lesions of the Hindbrain (Lateral Medullary Syndrome), Brain **53**:290, 1930.

11. Adamkiewicz, A.: Die Arterien des verlängerten Markes, Denkschr. d. k. Akad. d. Wissensch. Math-naturw. Kla. **57**:1, 1890.

12. Duret, H.: Sur la distribution des artères nourricières du bulbe rachidien, Arch. de physiol. norm. et path. **5**:97, 1873; Recherches anatomiques sur la circulation de l'encéphale, ibid. **6**:60, 316 and 664, 1874.

type of vascularity was, with some modifications, present on both sides in nine of the twelve cases studied. The anterior artery of the lateral parolivary fossa arises independently from the basilar artery as its most caudal branch (fig. 1) or together with the arteria cerebelli inferior anterior or with this artery and the arteria auditiva interna. The arteria fossae lateralis parolivaris intermedia arises as a direct branch from the vertebral artery (fig. 1). Sometimes not a single branch but two small branches of this kind may be present (fig. 2).

The posterior artery of the lateral parolivary fossa arises as a branch from the posterior inferior cerebellar artery (figs. 1 and 2).

This typical distribution of the arteries of the lateral parolivary fossa is also observed in cases in which the anterior inferior cerebellar artery is absent on one side (fig. 2), as was seen in two of the present cases. In both the anterior artery of the lateral parolivary fossa originated as an independent branch of the basilar artery. However, in one of them there was a large anastomosis with the arteria auditiva interna (fig. 2).

In three of our twelve cases the artery of the lateral parolivary fossa showed atypical distribution, which we, therefore, considered as an aberration from the norm. In two of these cases the posterior inferior cerebellar artery was missing on one side, and the entire length of the lateral parolivary area was supplied by only two arteries, namely, the anterior and the intermediate artery of the lateral parolivary fossa (fig. 3). The anterior artery of the lateral parolivary fossa originated in both these cases from the inferior anterior cerebellar artery and was abnormally long, reaching the caudal end of the lateral parolivary fossa. The intermediate artery or arteries of the lateral parolivary fossa originated from the vertebral artery. In one of the cases, one, and in the other, two of these arteries were present. In both cases these abnormalities were present on the right side, while the left side showed the blood supply typical of this region.

In one of the twelve cases the anterior artery of the lateral parolivary fossa was absent on one side. In this case the entire length of the lateral parolivary fossa was supplied by a long, large branch of the posterior inferior cerebellar artery (fig. 4), supplemented by a small intermediate artery of the lateral parolivary fossa.

(*B*) *Distribution of Arteries of the Lateral Parolivary Fossa Within the Area Parolivaris Lateralis of the Medulla.*—In five of our cases injection within the medulla oblongata was patchy and incomplete; therefore we did not include them in this part of the study. In seven of the twelve cases injection within the medulla oblongata was satisfactory. In four of the seven cases the anterior artery of the lateral parolivary fossa was injected—in two, directly and in two, by injecting the common trunk of this artery and the anterior inferior cerebellar artery. In another case the radicular artery of the acoustico-

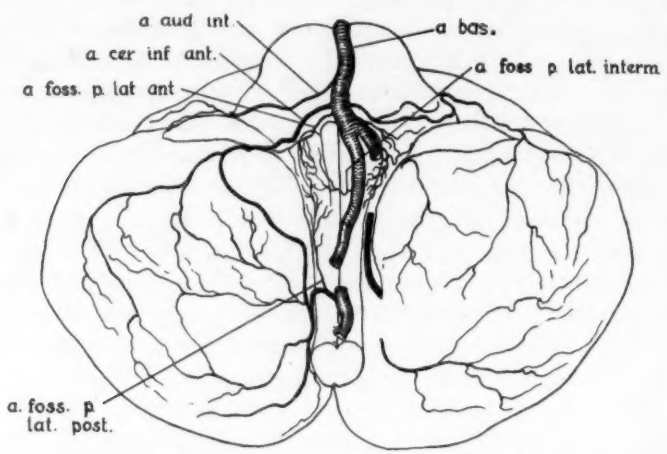

Fig. 1.—Normal distribution of arteries on the base of the medulla oblongata. The arteria fossae parolivaris lateralis anterior (*a. foss. p. lat. ant.*) is a direct branch of the basilar artery (*a. bas.*), caudal to the origin of the arteria cerebelli inferior anterior (*a. cer. inf. ant.*). The arteria fossae parolivaris lateralis posterior (*a. foss. p. lat. post.*) is a branch from the posterior inferior cerebellar artery; the arteria fossae parolivaris lateralis intermedia (*a. foss. p. lat. interm.*) arises from the vertebral artery.

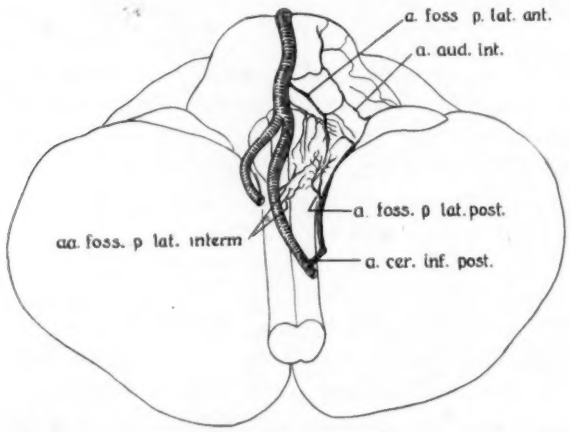

Fig. 2 (specimen 2).—Normal distribution of arteries on the base of the medulla oblongata in a case in which the left arteria cerebelli inferior anterior is absent. The arteria fossae parolivaris lateralis anterior arises as a direct branch from the basilar artery, caudal to the arteria auditiva interna, with which it shows anastomosis. The arteria fossae parolivaris lateralis posterior is a branch from the posterior inferior cerebellar artery (*a. cer. inf. post.*); the arteriae fossae parolivaris lateralis intermediae arise from the vertebral artery. Abbreviations are similar to those in figure 1.

facial nerve was injected. In an additional case the right posterior inferior cerebellar artery was injected. In a case in which the anterior artery of the lateral parolivary fossa was absent the posterior inferior cerebellar artery was injected on the same side with black material, and

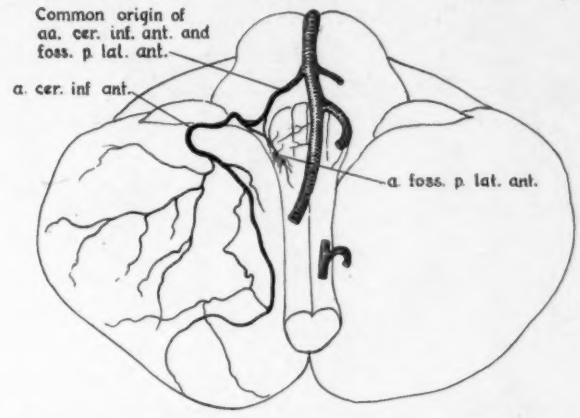

Fig. 3.—Absence of the right posterior inferior cerebellar artery and the posterior artery of the lateral parolivary fossa. The entire lateral parolivary fossa is supplied by an abnormally long arteria fossae parolivaris lateralis anterior (*a. foss. p. lat. ant.*), supplemented by a small arteria fossae parolivaris lateralis intermedia.

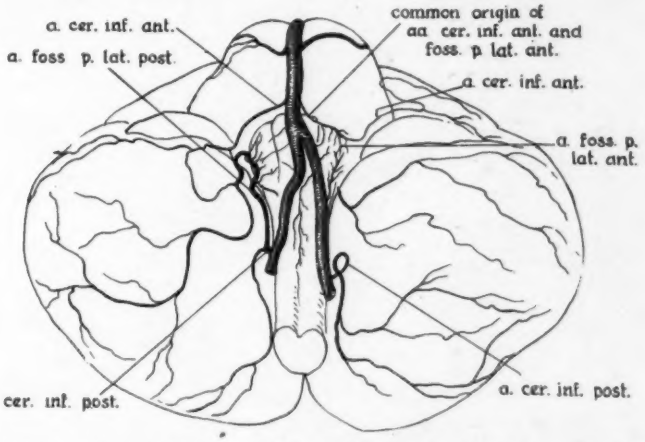

Fig. 4 (specimen 7).—Absence of the right arteria fossae parolivaris lateralis anterior. The entire length of the lateral parolivary fossa is supplied by a long, large posterior artery of the lateral parolivary fossa (*a. foss. p. lat. post.*), a branch of the posterior inferior cerebellar artery (*a. cer. inf. post.*), supplemented by one intermediate artery of the lateral parolivary fossa.

the vertebral artery of the other side, with red material. In the following section we shall summarize our results.

1. Injection of Anterior Artery of the Lateral Parolivary Fossa: In all four cases of this group the anterior part of the lateral parolivary area of the medulla oblongata was well injected; in two cases the anterior part consisted of the anterior third, in one case of the anterior fourth and in another of the entire anterior half of the area.

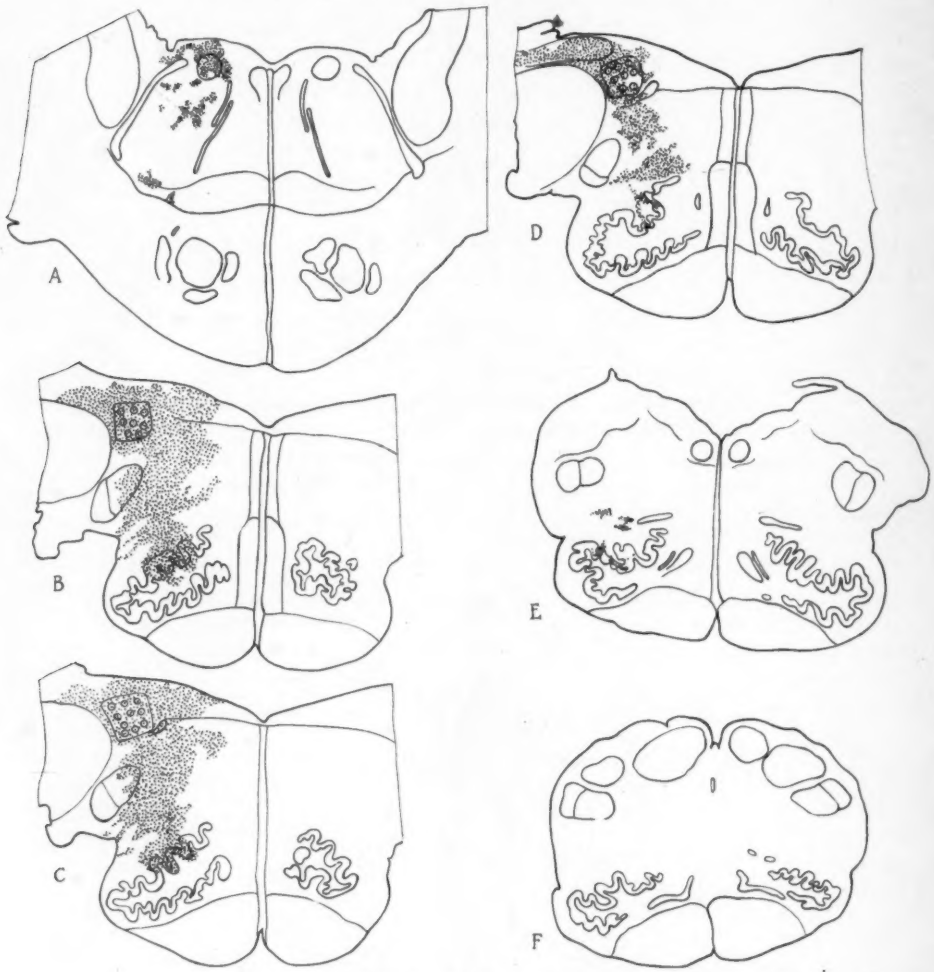

Fig. 5 (specimen 1).—Injection of the anterior artery of the left lateral parolivary fossa. Diagrams of a series of cross-sections of the pons and medulla oblongata. Injected areas are stippled. Enlargement, 3.

The injected area was largest and the injection most intensive in the two cases of this group in which the anterior artery of the lateral parolivary fossa was a direct branch of the basilar artery (specimens 1 and 2; figs. 5, 6 and 7). In both these cases the injection covered a wedge-shaped field of the medulla oblongata inserted between the

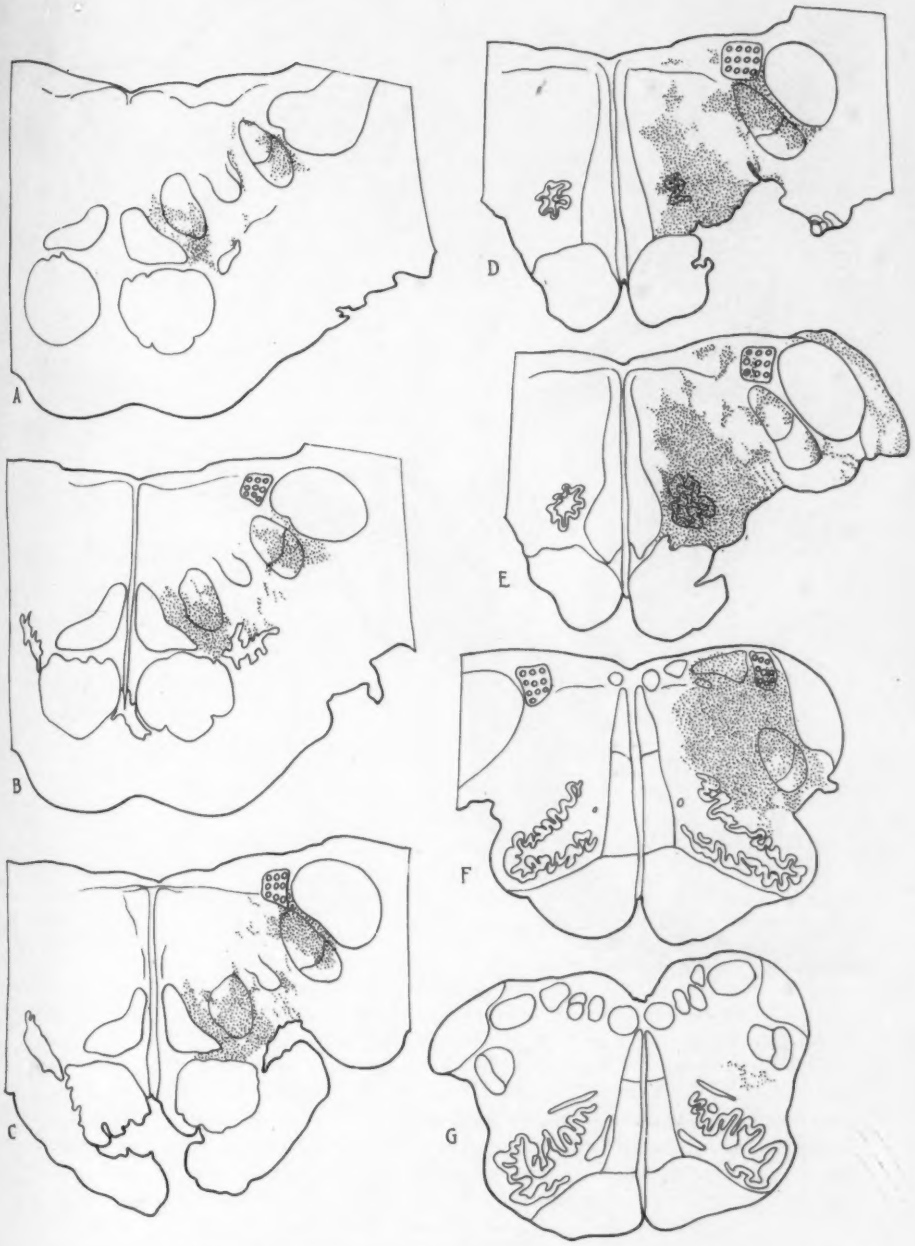

Fig. 6 (specimen 2).—Injection of the anterior artery of the right lateral parolivary fossa. Diagrams of a series of cross-sections of the pons and medulla oblongata. Injected areas are stippled. Enlargement, about 3.

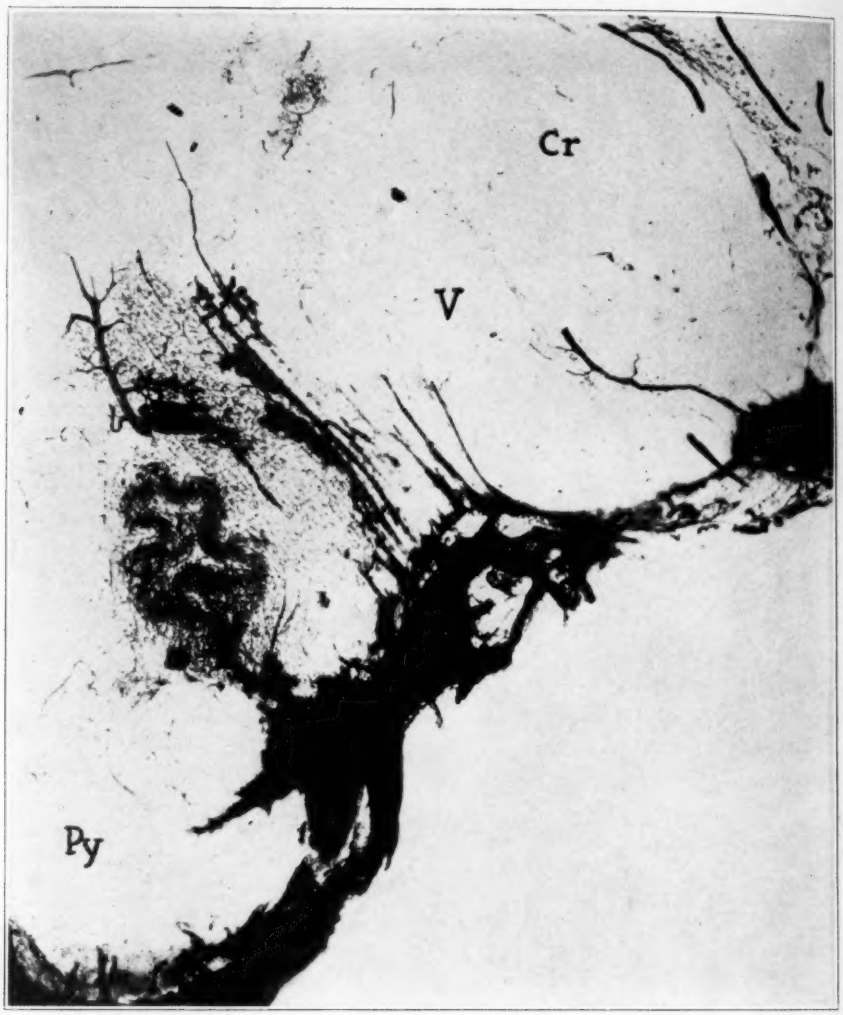

Fig. 7 (specimen 2).—Injection of the anterior artery of the right lateral parolivary fossa. Cross-section of the anterior part of the medulla oblongata.

Photomicrograph of the section shown in diagram *E* in figure 6. The following structures are injected: The anterior tip of the inferior olive and the lateral parolivary area, including: the nucleus ambiguus (velum palatinum), the central tegmental, spinotectothalamic, rubroreticulospinal and ventral spinocerebellar tracts, the fibrae arcuatae internae and part of the central and dorsolateral reticulated substance. Besides this dense area of injection, there is slight injection of the ventral and dorsal cochlear nuclei, a small lateral part of the nucleus vestibularis triangularis and very small parts of the root and the nucleus of the descending trigeminus nerve, as well as a few vessels within the nucleus of Deiters. *Cr* indicates the corpus restiforme; *V*, the descending portion of the trigeminus nerve, and *Py*, the pyramidal tract. Enlargement 8½.

inferior olive and the restiform body, which in both cases included also the anterior tip and an adjacent small part of the dorsal leaf of the inferior olive, the central and dorsolateral part of the reticulated substance and some of the nuclei on the floor of the fourth ventricle. The point of the wedge pointed in either a dorsomedial or a lateroventral direction. The corpus restiforme was free from injection. The nuclei and tracts which the injection included are listed in the table.

In the two cases in which the anterior artery of the lateral parolivary fossa was a branch of the anterior inferior cerebellar artery, the injected area in the medulla oblongata was markedly smaller (specimens 3 and 4; fig. 8 *A* and *B*). In these cases the anterior part of the lateral parolivary area was injected; the injected area, however, was somewhat

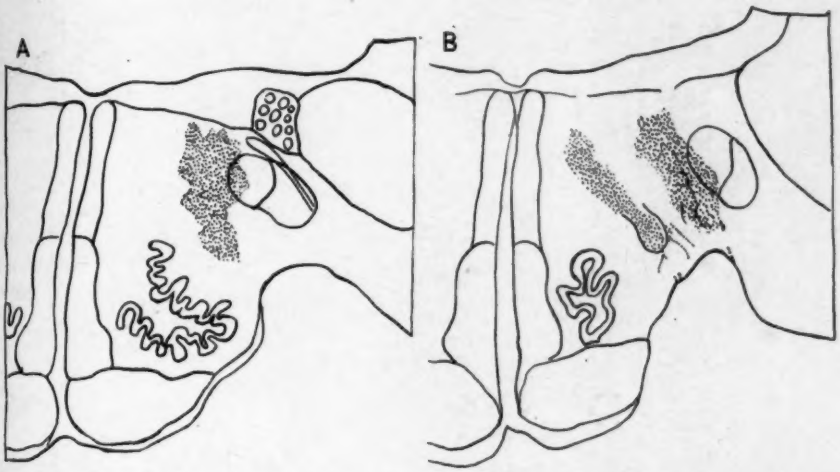

Fig. 8.—Injection of the common trunk of the anterior inferior cerebellar artery and the anterior artery of the lateral parolivary fossa. Diagrams (enlargement, 3.3) of cross-sections of the anterior part of the medulla oblongata. The injected area is stippled. *A* was drawn from specimen 3, and *B*, from specimen 4.

smaller than in the first two cases and was ovoid rather than wedge-shaped. It included in one case the anterior third and in the other the anterior fourth of the lateral parolivary area (for the detailed distribution see the accompanying table).

2. Injection into the Common Branch of the Arteria Auditiva Interna and the Radicular Artery of the Acoustic Nerve: In this case the inferior olive and the lateral parolivary area were completely free from injection. The root of the eighth nerve, the nuclei cochlearis dorsalis and ventralis and the corresponding level of the restiform body were well injected, and also some of the large arterioles which accompany the outgrowing root of the seventh nerve. There was only

Nuclei and Tracts Included in the Area of Injection

Injected Nuclei and Tracts	Anterior Artery of Lateral Parolivary Fossa				Common Branch of Arteria Auditiva Interna and Radicular Artery of Acoustic Nerve	Posterior Inferior Cerebellar Artery	Right Posterior Inferior Cerebellar Artery, in Case of Absence of Right Anterior Artery of Lateral Parolivary Fossa	Left Vertebral Artery
	Specimen 1 (Fig. 5)	Specimen 2 (Figs. 2, 6 and 7)	Specimen 3 (Fig. 8A)	Specimen 4 (Fig. 8B)	Specimen 5 (Figs. 9 and 10)	Specimen 6 (Figs. 11 and 12)	Specimen 7 (Figs. 4, 13 and 14)	Specimen 7 (Figs. 4, 13 and 14)
Restiform body	0	0	0	0	+	+	+	0
Inferior olive	Anterior tip and adjacent part of dorsal leaf +	Anterior tip and adjacent part of dorsal leaf +	0	0	0	Posterior part of dorsal leaf +	Part of dorsal leaf +	Ventral leaf +
Nucleus cochlearis ventralis	0	Part +	0	0	+	Part +	Caudal part +	0
Nucleus cochlearis dorsalis	Medial part +	+	0	0	+	Part +	+	0
Cochlear and vestibular roots	0	0	0	0	+	Part +	Caudal part +	0
Root of seventh nerve	0	0	0	0	+	0	0	0
Nucleus vestibularis descendens	+	+	0	0	0	+	Part +	0
Nucleus vestibularis triangularis	Lateral part and anterior tip +	Laterocaudal part +	0	0	0	+	Part +	Medio-oral part +
Nucleus of Deiters	Caudal part +	Small part of caudal portion +	0	0	Part +	+	Part +	0
Root of descending trigeminus nerve	0	Part +	0	0	0	+	+	0
Nucleus gelatinosus of descending trigeminus nerve	Part +	Part +	Small medial part +	Small medial part +	0	+	+	0
Nucleus glossopharyngeus	Oral part +	Middle part +	0	0	0	+	+	0

Nucleus dorsalis nervi vagi	0	0	0	0	0	+	+	0
Nucleus hypoglossus	0	0	0	0	0	Capsule and lateral part +	0	+
Nucleus praepositus nervi hypoglossi	0	0	0	0	0	Capsule and part +	0	+ (Bilateral)
Posterior longitudinal bundle	0	0	0	0	0	Laterodorsal part +	0	+ (Bilateral)
Nuclei of posterior column	0	0	0	0	0	+	+	0
Pyramidal tract	0	0	0	0	0	0	0	+
Medial lemniscus	0	0	0	0	0	0	0	+ (Bilateral)
Predorsal bundle	0	0	0	0	0	0	0	+ (Bilateral)
Nucleus funiculi teretis	0	0	0	0	0	0	0	+ (Bilateral)
Nucleus abducens	Part +	0	0	0	0	0	0	Part +
Lateral parolivary area, including the following nuclei and tracts:	Anterior third +	Anterior half +	Anterior third +	Anterior fourth +	0	Posterior two-thirds +	Entire length +	0
Nucleus ambiguus	+	+	+	+	0	+	+	0
Nucleus facialis	0	0	Caudal part +	Caudal part +	0	0	0	0
Tractus spinotectalis et thalamicus	+	+	Part +	+	0	+	+	0
Tractus rubroreticulospinalis	Part +	+	0	+	0	+	+	0
Tractus spinocerebellaris ventralis	Part +	Part +	0	0	0	+	+	0
Tractus tegmenti centralis	Part +	+	Part +	0	Part +	+	+	0
Dorsolateral reticulated substance, in prolongation of lateral parolivary area	+	+	+	+	0	+	+	0
Central reticulated substance, in dorsomedial prolongation of lateral parolivary area	+	+	0	+	0	+	+	0
Fibrae arcuatae internae	+	+	+	+	0	+	+	+ (In midline)

slight injection of the lateral part of the nucleus of Deiters (specimen 5, table; figs. 9 and 10).

3. Injection of the Posterior Inferior Cerebellar Artery: The posterior two thirds of the lateral parolivary region and the upper leaf

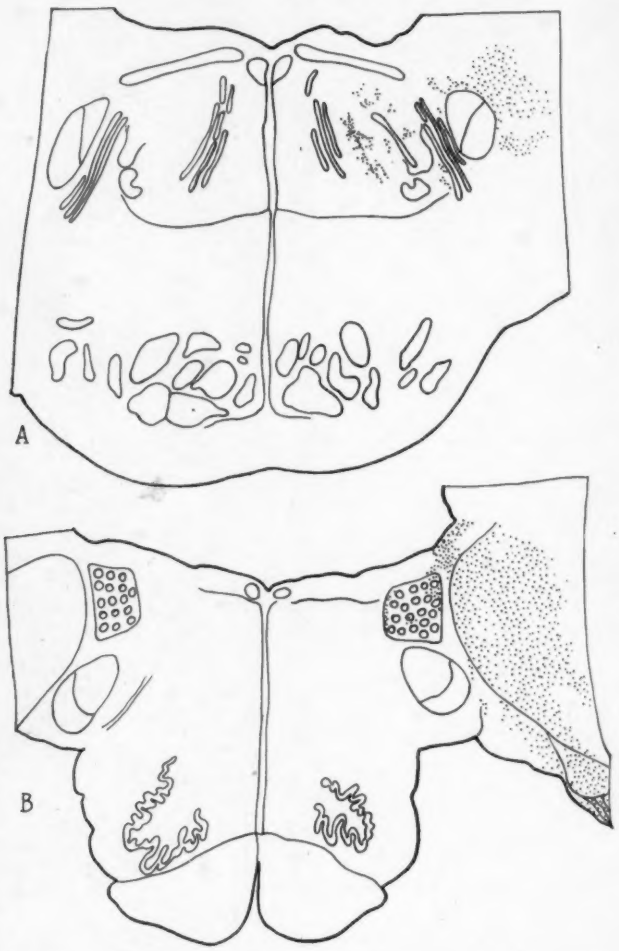

Fig. 9 (specimen 5).—Injection into the common trunk of the arteria auditiva interna and the radicular artery of the acoustic nerve on the right. Diagrams of cross-sections of the pons and medulla oblongata. Injected areas are stippled. Enlargement, about 3.

of the inferior olive were well injected, in addition to the dorsolateral region of the medulla oblongata.

The anterior third of the lateral parolivary area, however, as well as the anterior third of the inferior olive, was not injected (specimen 6, table; figs. 11 and 12).

4. Injection of Black Material into Posterior Inferior Cerebellar Artery in Case of Absence of Anterior Artery of Lateral Parolivary Fossa, with Injection of Contrasting (Red) Material into Contralateral Vertebral Artery Near Junction with Basilar Artery, Distal to Origin of Posterior Inferior Cerebellar Artery and Intermediate Artery of Lateral Parolivary Fossa: In this case the anterior artery of the

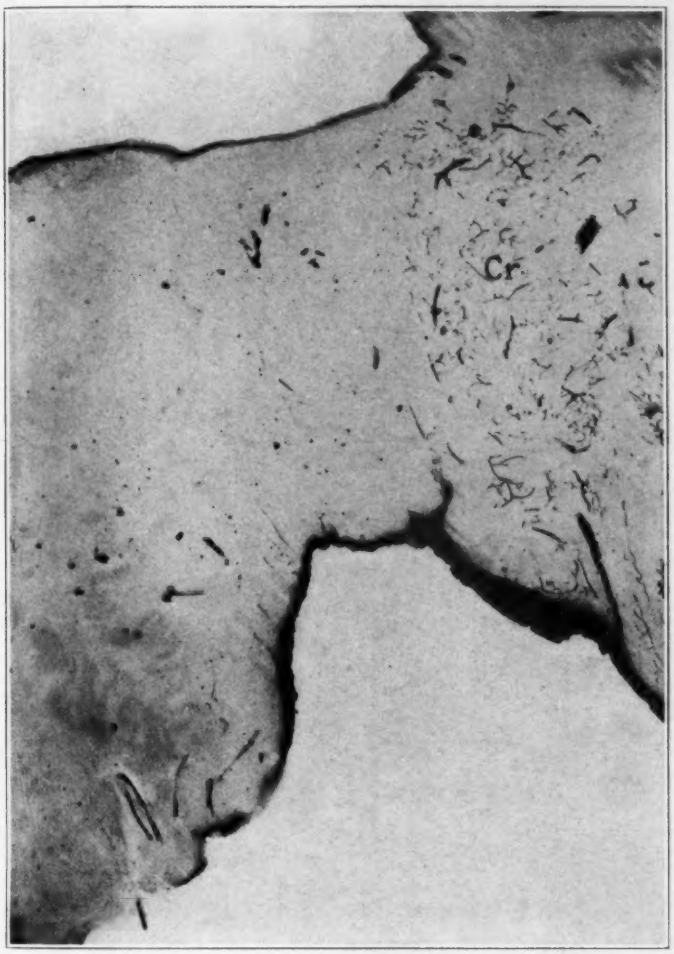

Fig. 10 (specimen 5).—Injection into the common trunk of the arteria auditiva interna and the radicular artery of the acoustic nerve on the right. Cross-section of the anterior part of the right half of the medulla oblongata. Photomicrograph of the section shown in diagram *B* in figure 9. *Cr.* indicates the corpus restiforme. Enlargement, 6½.

lateral parolivary fossa was absent on the right. The intermediate artery of the lateral parolivary fossa was rudimentary on the same

side. The entire length of the lateral parolivary fossa appeared to be supplied by a long, large branch of the posterior inferior cerebellar artery—in other words, by an overdeveloped posterior artery of the lateral parolivary fossa (specimen 7; fig. 4). The right posterior inferior cerebellar artery was injected with black material. Contrasting injection of red material was made into the left vertebral artery, near its junction with the basilar artery.

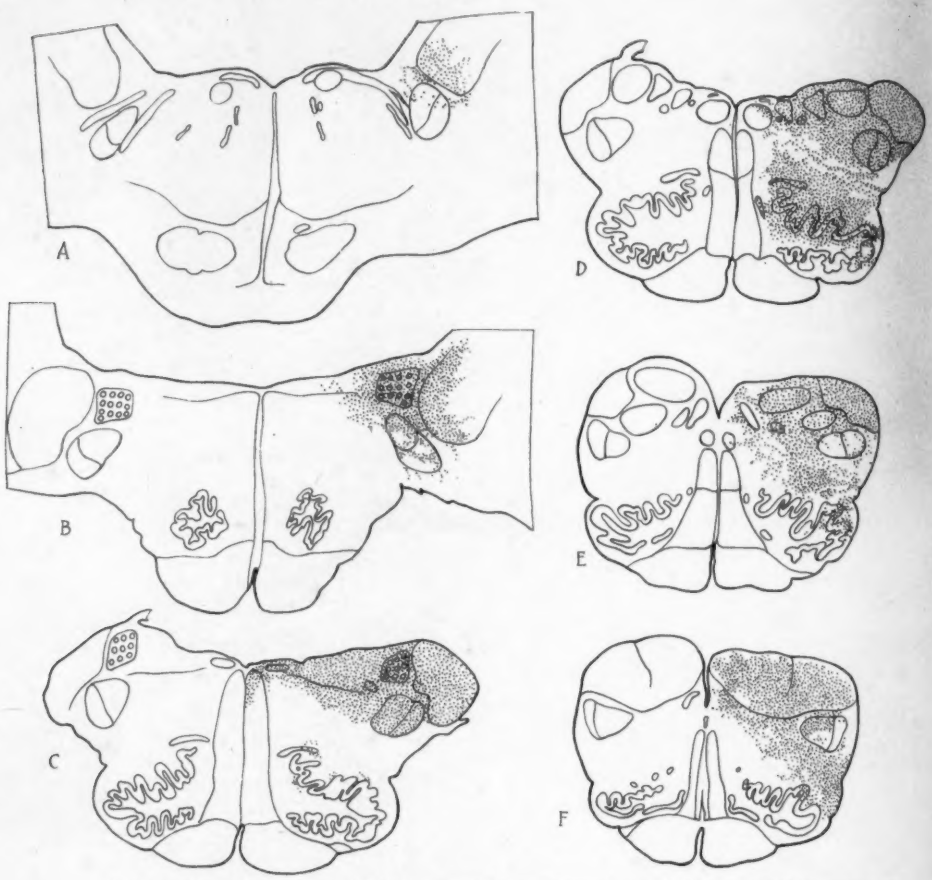

Fig. 11 (specimen 6).—Injection of the right posterior inferior cerebellar artery. Diagrams of a series of cross-sections of the medulla oblongata and pons. Injected areas are stippled. Enlargement, about 3.

In this case injection of black material into the right posterior inferior cerebellar artery in the medulla covered the entire length of the right lateral parolivary area (specimen 7, table; figs. 13 and 14).

At the level of the oral half of the medulla oblongata injection of red material through the left vertebral artery covered the left paramedian area; in the caudal half of the pons, injection of red material

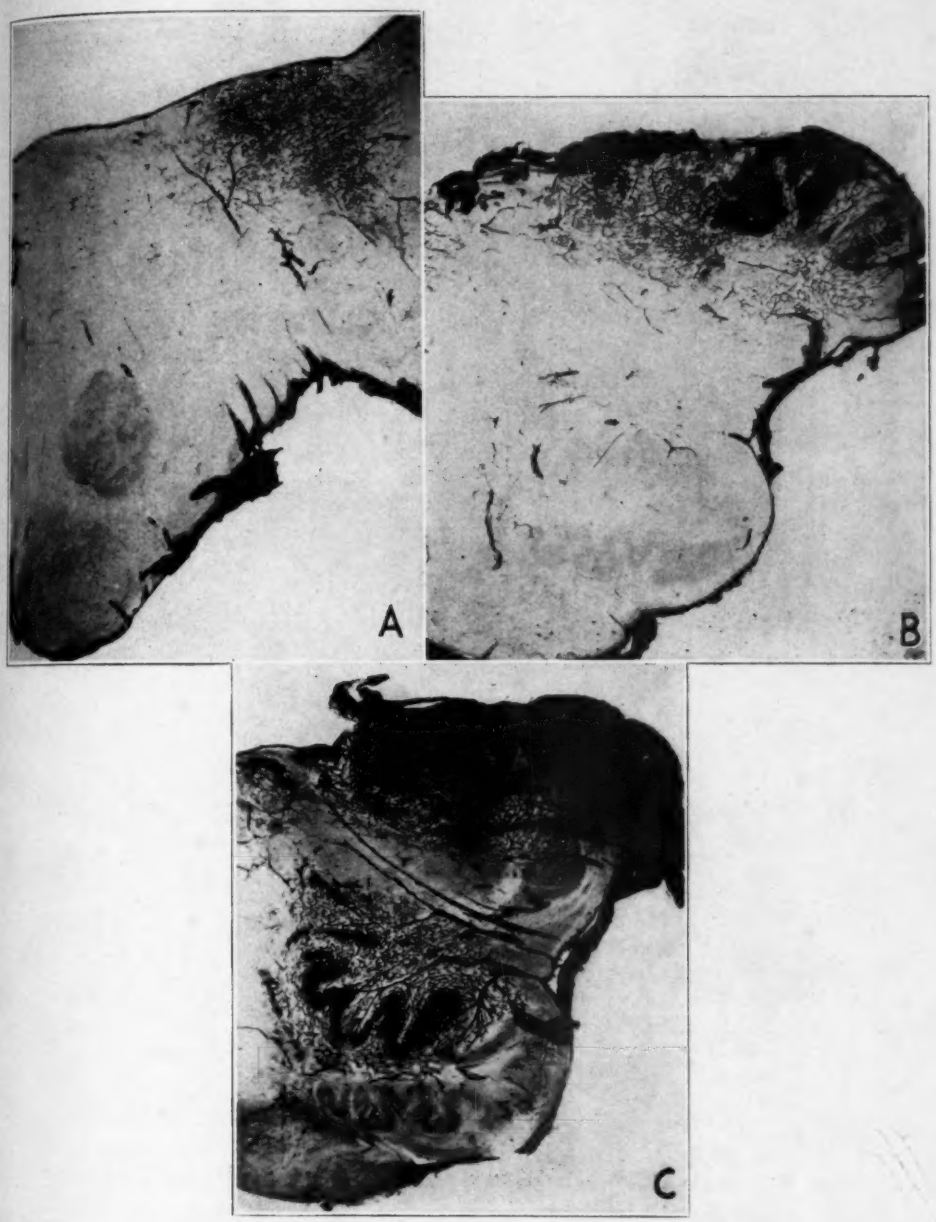

Fig. 12 (specimen 6).—Injection of the right posterior inferior cerebellar artery. Series of cross-sections of the medulla oblongata. Photomicrographs of sections shown in diagram *B*, *C* and *D* in figure 11. Enlargement, 6.

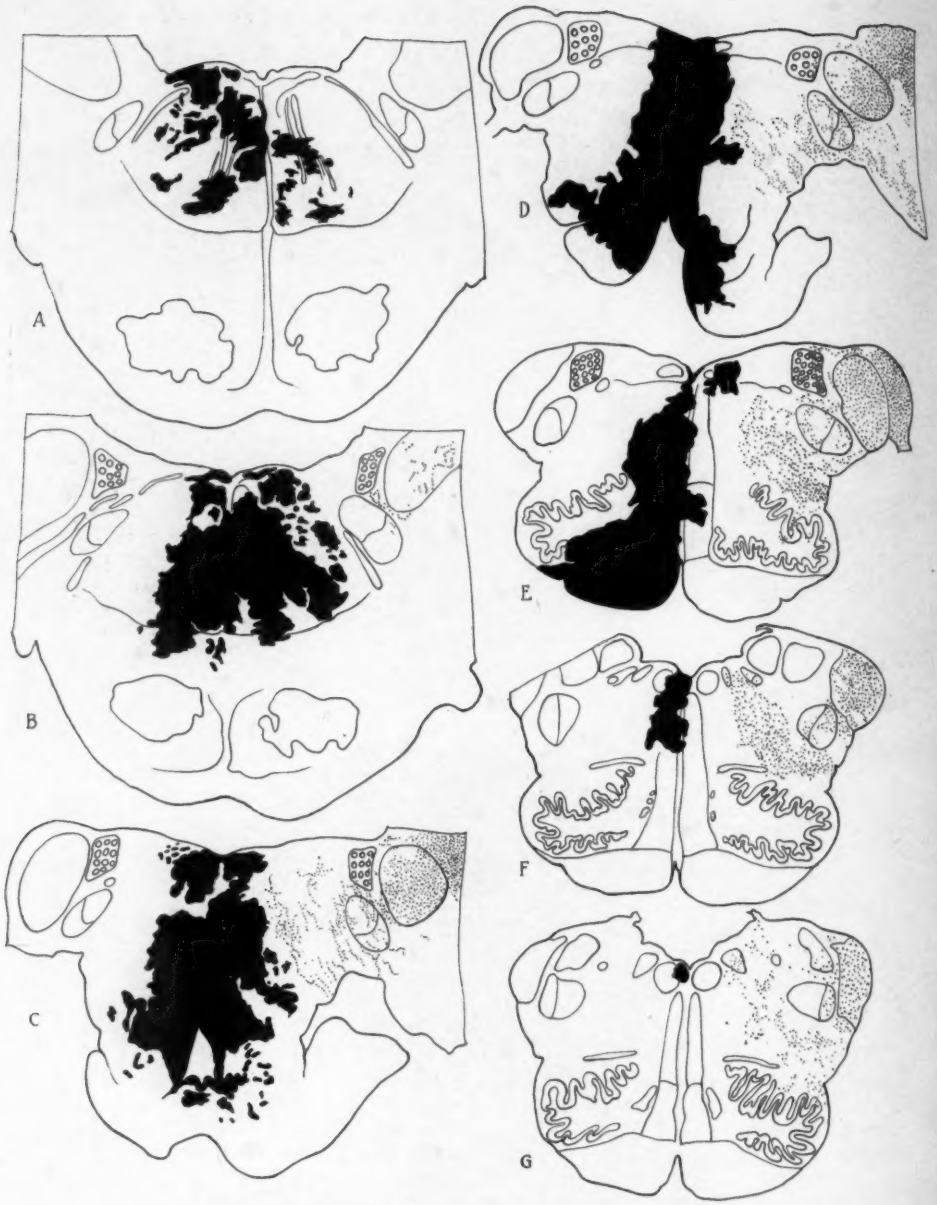

Fig. 13 (specimen 7).—Injection of red material into the left vertebral artery, near its junction with the basilar artery, and of black material into the right posterior inferior cerebellar artery, in a case of absence of the right anterior artery of the lateral parolivary fossa (see figure 4). Diagrams of a series of cross-sections of the medulla oblongata and pons. Injection of red material (through the left vertebral artery) is indicated in solid black, and that of black material (through the right posterior inferior cerebellar artery), by stippling. Enlargement, about 3.

covered both paramedian areas of the tegmentum (specimen 7, figs. 13 and 14).

COMMENT

1. The arterial supply of the lateral parolivary area of the medulla oblongata was studied by injection of the smallest extramedullary arterial branches. Though there is a great deal of individual variability as to the size and course of these branches and, correspondingly, as to the size, location and shape of the injected areas, the injection in cases in which the vascular pattern was similar always covered well defined, constant and rather sharply circumscribed areas. There was little extravasation of injected material into the neighboring veins or arteries and almost none into surrounding capillary nets, in spite of their

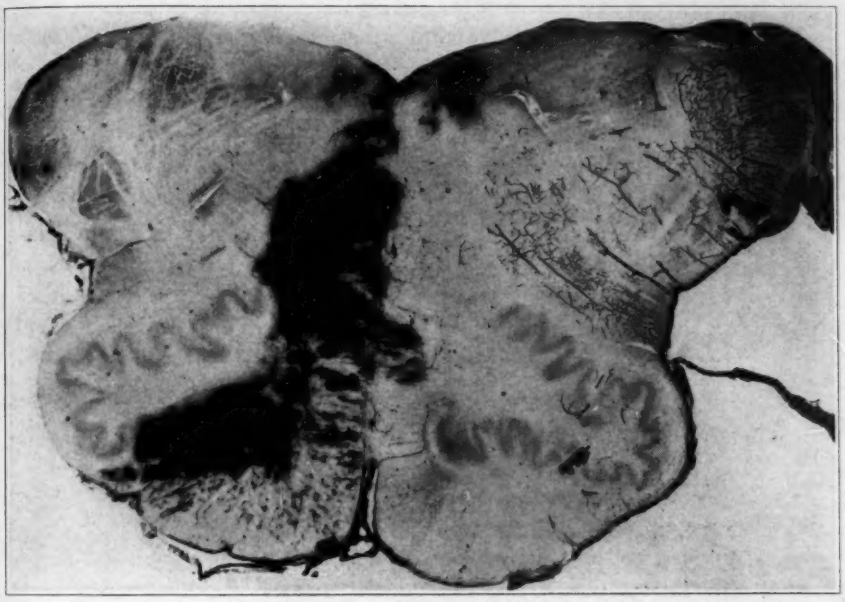

Fig. 14 (specimen 7).—Injection of contrasting material into the left vertebral and the right posterior inferior cerebellar artery in a case of absence of the right anterior artery of the lateral parolivary fossa. Photomicrograph of the section shown in diagram *E* in figure 13. Enlargement, about 5.

obvious anatomic continuity. This suggests that under the conditions of postmortem injection, as applied in our study, the small arteries of the human medulla oblongata behave like end-arteries in Cohnheim's sense, though anastomoses are observed among the meningeal arteries of a larger order of magnitude, as well as within the capillary network (Wislocki and Campbell [13]).

13. Wislocki, G. B., and Campbell, A. C. P.: Personal communication to the authors concerning work in progress.

2. The lateral parolivary area of the medulla oblongata and its prolongation dorsally into the reticulated substance up to the ventral border of the triangular nucleus are supplied in the anterior part (anterior third, fourth or half) by the anterior artery of the lateral parolivary fossa (the *artère de la fossette latérale* of Foix, Hillemand and Schalit). In the posterior two-thirds (three-fourths or half) it is supplied by the posterior artery of the lateral parolivary fossa, which is a branch of the posterior inferior cerebellar artery, supplemented by one or two small direct branches from the vertebral artery (intermediate arteries of the lateral parolivary fossa).

The arterial supply of the anterior part of the lateral parolivary area in most cases includes also a part of the nucleus of the descending trigeminal nerve and part of the dorsal leaf of the inferior olive, as well as parts of the descending vestibular nucleus, the nucleus triangularis and the nucleus cochlearis dorsalis. It never includes all or parts of the restiform body. In case of absence of the posterior artery of the lateral parolivary fossa, the entire lateral parolivary area and its dorsal prolongation into the central and dorsal reticular substance are supplied by the anterior artery of the lateral parolivary fossa.

3. The restiform body, the root and the major part of the nucleus of the descending fifth nerve, the major part of the descending vestibular nucleus and of the nucleus triangularis, the nucleus glossopharyngeus and nucleus dorsalis nervi vagi, the posterior two thirds of the lateral parolivary area, including that part of the dorsal leaf of the inferior olive, are irrigated by the posterior inferior cerebellar artery. In case of absence of the anterior artery of the lateral parolivary fossa, the posterior inferior cerebellar artery also supplies the anterior part of the lateral parolivary area and its dorsomedial prolongation into the reticulated substance.

SUMMARY

1. The lateral parolivary area of the human medulla oblongata is supplied in its anterior third (half or fourth) by the anterior artery of the lateral parolivary fossa (a branch of the basilar artery). In its posterior two-thirds (half or three-fourths), it is supplied by the posterior artery of the lateral parolivary fossa (a branch from the posterior inferior cerebellar artery), supplemented by one or two intermediate arteries of the lateral parolivary fossa (branches from the vertebral artery).

2. In case of absence of either the anterior or the posterior artery of the lateral parolivary fossa associated with rudimentary development of the intermediate artery or arteries, either the anterior or the posterior artery of the lateral parolivary fossa supplies the entire lateral parolivary area.

SPECIAL ARTICLES

OXYGEN METABOLISM IN SCHIZOPHRENIA

R. G. HOSKINS, M.D.
BOSTON

During the past decade the research service of the Worcester State Hospital has carried out a variety of studies which directly or indirectly bear on the problem of oxygen metabolism in schizophrenic psychosis. It is my purpose in this paper to present a summary of the findings. I am indebted to numerous colleagues for permission to make use of their data, some of which have not yet been published.

It should be emphasized that the evidence to be cited represents trends rather than characteristic definition of the schizophrenic group as a whole. No implication is intended that the disorder constitutes an entity. In the distributions there is considerable overlapping of the levels found in the patients and those in the subjects used as controls. The means of the distributions, however, are significantly different.

Special interest attaches to the topic discussed because of the fact, which has been pointed out by McFarland [1] and others, that deficiencies in oxygen assimilation may bring about a variety of manifestations in nonpsychotic subjects that are highly suggestive of the symptomatology of schizophrenia. Data from three sources are available: the experiences of aviators, of mountain climbers and of subjects studied experimentally in closed chambers under reduced oxygen pressures. From the individual manifestations that have been reported in such subjects one could readily synthesize a picture that would be accepted unquestioningly as that of typical schizophrenia. Among the demonstrated results of low oxygen tensions are limitation in the field of attention; perseveration; apathy; depression of spirits; inappropriateness of affect with silly laughter; poor judgment, often with a high opinion of mediocre performances; obliviousness to obvious danger; loss of self-control; anxiety; excitement without apparent cause; uncontrollable emotional outbursts with laughing, shouting, singing, weeping and dangerous violence; abusiveness; insidious loss of power of decision and unwillingness to bear responsibility, and gradual failure of sane judgment and the "sense of fitness of things." McFarland has cited such manifestations as evidence of general loss of "integration."

From the Memorial Foundation for Neuro-Endocrine Research and the Research Service of the Worcester State Hospital, Worcester, Mass.

1. McFarland, R. A.: The Psychological Effect of Oxygen Deprivation (Anoxemia) on Human Behavior, Arch. Psychol., 1932, no. 145.

It thus appears that whether or not defective oxygen metabolism is an important factor in schizophrenia, numerous classic manifestations of that condition could be brought about by such an agency. The fact that many normal subjects give schizoid reactions to oxygen deprivation cannot, however, be cited as proof of the oxygen deficiency theory of schizophrenia, for there is no certainty that prolonged exposure to lesser degrees of oxygen lack would have an effect equivalent to that of more acute deficiency over a shorter period. The crux of the problem, therefore, largely is to determine whether or not defective tissue oxygenation does occur.

The actual rate of oxygen consumption—often miscalled the "basal metabolic rate"—of schizophrenic persons has been studied by several investigators, most of whom have reported a significant depression below standard normal rates. To obtain a true basal rate in most schizophrenic persons is difficult, if not impossible. Unless the patient has been habituated to the test procedure, he is not entirely at ease, and a certain element of increase is registered in the oxygen uptake that is dependent merely on psychomotor tension. The true basal rate in most cases is probably considerably lower than the rate actually determined. In previous publications [2] my associates and I have reported a mean rate about 11 per cent below that of textbook standard. More recently, we have had opportunity to restudy the problem, utilizing as controls normal subjects employed to live in the hospital with the patients and to undergo the same tests as they. This most recent sample of thirty controls and thirty male schizophrenic patients of similar ages and states of physical health has confirmed the previous findings. The members of both groups were tested repeatedly until they became habituated to the procedures. As would be anticipated, these rehearsals resulted in lower rates for the controls than the prediction from conventional standards (fig. 1). The average mean rate was 93 per cent of prediction, and that for the patients, 86 per cent. Translated into terms of the ad hoc controls, the average mean rate for schizophrenic patients was 7.5 per cent below prediction. The average minimum rate for the patients was 74 per cent, and that for the controls, 79 per cent of prediction; i. e., the rate for the patients was 6.3 per cent below that for the controls. Demonstrably, then, the average schizophrenic subject consumes less oxygen than normal.

As to how the lowered oxygen consumption is brought about more information is needed. Golla and his associates [3] studied the compara-

2. Hoskins, R. G., and Sleeper, F. H.: Basal Metabolism in Schizophrenia, Arch. Neurol. & Psychiat. **21**:887 (April) 1929. Hoskins, R. G.: Oxygen Consumption ("Basal Metabolic Rate") in Schizophrenia, ibid. **28**:1346 (Dec.) 1932.

3. Golla, F.; Mann, S. A., and Marsh, R. G. B.: The Respiratory Regulation in Psychotic Subjects, J. Ment. Sc. **74**:443 (July) 1928.

tive sensitivity to carbon dioxide of the respiratory center of schizophrenic patients and that of normal subjects. When the percentage of carbon dioxide in the inspired air was increased to 2 per cent, the ventilation of the lungs of normal subjects was definitely stimulated, whereas six of seven schizophrenic patients failed to show the increase. If the resting schizophrenic patient is less than normally sensitive to stimulating metabolites, he might be expected to show chronic underventilation of the lungs, and this, if sufficient in degree, would result in chronic underoxidation of the arterial blood.

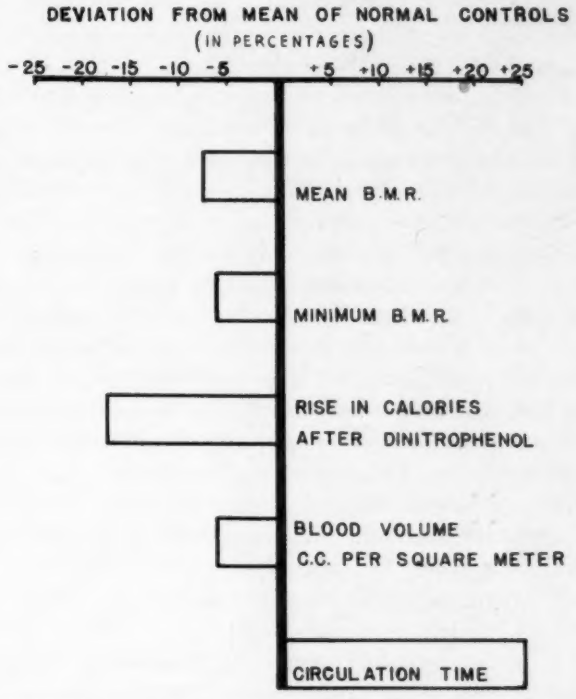

Fig. 1.—Deviations from the normal noted in the average findings for thirty schizophrenic subjects as compared with those for thirty normal persons tested under comparable conditions.

Whether the oxygen tension in the arterial blood is significantly reduced is open to direct observation. In the investigations which my colleagues have carried on,[4] the average degree of oxygen saturation has been found to be the same in patients and in subjects used as controls, but this similarity may have been due to failure to avoid a certain amount

4. Looney, J. M., and Freeman, H.: The Oxygen and Carbon Dioxide Content of the Arterial and Venous Blood of Schizophrenic Patients, Arch. Neurol. & Psychiat., to be published.

of stimulation of the subjects during the process of collecting the samples of blood. According to McFarland,[5] significant lowering of the oxygen content of the arterial blood can be demonstrated in a certain proportion of schizophrenic patients if one avoids arousing the subjects.

A deficiency of tissue oxidation could arise from either of two mechanisms: (*a*) failure of the blood to carry an adequate amount of oxygen to the tissues, or (*b*) inability of the tissues to assimilate a normal amount of oxygen when the supply is adequate. Of course, both mechanisms might operate simultaneously.

A defective degree of oxygen transport, however, might arise even though the arterial blood contained the normal proportion of oxygen, should the volume of the blood be significantly reduced or the celerity of its circulation lessened. As a matter of fact, Looney and Freeman[6] have found that the blood volume of the schizophrenic person, when referred to the surface area, is significantly less than that of normal subjects used as controls. When the subjects were matched by "nutritional index," the difference was not seen. Hence, the lowered blood volume frequently found in schizophrenic persons may represent a special aspect of lowered general nutrition. Even so, however, the findings would seem to be significant if it is true, as is commonly assumed, that the surface area is the best reference datum to which to relate metabolic activity. Reduction of the blood volume of schizophrenic persons has more recently been reported by Finkelman and Haffron.[7]

Determination of the representative circulatory rate in the schizophrenic person requires attention to the conditions attending the test. The cardiovascular system is exquisitely under sympathetic control, and both excitement and pain are sympathetic stimulants. To secure reliable results, therefore, the procedure of determining the circulatory rate must be carried out without arousing the patient. For such studies patients who are thoroughly accustomed to test procedures offer special advantage. A possible stimulant that must be taken into account is the substance that is used to afford an index of the circulation rate. Unless it is free from stimulating or sensitizing qualities, only a single determination can be made at each session. Freeman[8] made a study of the circulatory rate in schizophrenic patients and and in normal subjects serving as controls, using the sodium cyanide method. The drug

5. McFarland, R. A.: Personal communication to the author.

6. Looney, J. M., and Freeman, H.: Volume of Blood in Normal Subjects and in Patients with Schizophrenia, Arch. Neurol. & Psychiat. **34**:956 (Nov.) 1935.

7. Finkelman, I., and Haffron, D.: Observations on the Circulating Blood Volume in Schizophrenia, Manic-Depressive Psychosis, Epilepsy, Involutional Psychosis and Mental Deficiency, Am. J. Psychiat. **93**:917 (Jan.) 1937.

8. Freeman, H.: The Arm-to-Carotid Circulation Time in Normal and Schizophrenic Subjects, Psychiatric Quart. **8**:290 (April) 1934.

is injected at the elbow, and when it reaches the carotid sinus, it stimulates an afferent mechanism that causes the patient to gasp. Freeman found that the average arm to carotid interval for seventy-three schizophrenic patients in the resting, postabsorptive state was 25.6 seconds and, again, for fifty-two of these subjects four months later, 27.9 seconds, while that for twenty-six control subjects studied under comparable conditions was 21.9 seconds. Under nonbasal conditions the difference disappeared, the rate for the patients reaching the normal level. Thus it appeared that the blood of the average schizophrenic patient in the resting state moves through the tissues only about 80 per cent as rapidly as the blood of the average nonpsychotic person.

It appears, then, that the schizophrenic person in the unstimulated state—and this is largely his representative state—is under a handicap in the operation of the chief factors determining oxygen transport. However, there is evidence for the existence of other disabilities having to do with oxygen assimilation. Looney and Freeman [4] have recently reported on a study of the oxygen and carbon dioxide contents of the arterial and the venous blood of schizophrenic patients and normal subjects used as controls determined under basal conditions. It appeared that, despite the slowing in the circulatory rate of 20 per cent, with the correspondingly longer exposure of the blood to the reducing tissues, the schizophrenic patient succeeded in abstracting no more oxygen than did the control subject. Furthermore, the amount of carbon dioxide contributed to the blood stream was usually less than normal. It appears, therefore, that there may be a defect in the tissue respiration itself.

Another abnormal relationship that has been detected in our investigations is that between the glutathione and the lactic acid of the blood. So far only seventeen patients and seventeen control subjects have been studied, but the results are so striking as to justify brief notice in advance of more detailed publication. In tissue respiration glutathione can serve as an intermediary body to facilitate the assimilation of oxygen. The mean levels of glutathione in the blood of schizophrenic and those in normal subjects were found to be quite similar. In the normal subjects the levels for glutathione and those for lactate varied quite independently; i. e., neither appeared to be sensibly dependent on the other. In the schizophrenic group, however, a rather close relationship between the two substances was shown (fig. 2). When the glutathione was high the lactate was low and vice versa. Apparently, then, the schizophrenic person is forced even during rest to use an accessory mechanism on which the normal subject is not dependent. This dependence on glutathione obviously suggests that other oxidative mechanisms are defective. The defect might be either a lack of positive oxidative catalysts or the presence of one or more negative catalysts.

That the schizophrenic person is actually handicapped in his oxygen uptake is directly indicated by his reactions to thyroid. It is an empirical observation that clinical "hyperthyroidism" seldom, if ever, develops in schizophrenic subjects.[9] Furthermore, as Sleeper and I[10] reported several years ago, the average schizophrenic person is remarkably resistant to thyroid medication. Doses of 20 grains (0.129 Gm.) of desiccated

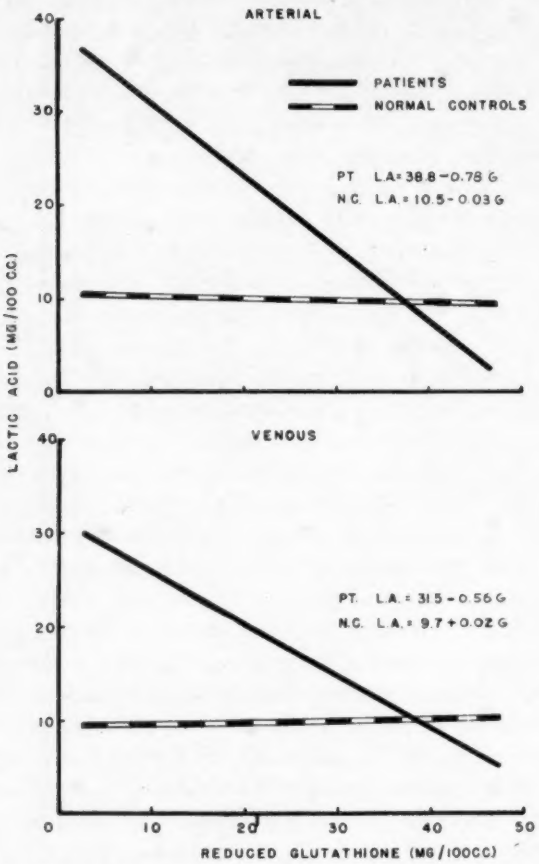

Fig. 2.—Relationship between the lactic acid content of the blood and the amount of reduced glutathione in seventeen schizophrenic and seventeen normal subjects. The regression equations representing the relationships are included in the graphs. *Pt.* indicates patients; *N.C.*, normal controls; *L.A.*, lactic acid, and *G*, reduced glutathione.

9. Deuticke, P.: Ein seltener Fall von Morbus Basedow, Wien. klin. Wchnschr. **42**:1475 (Nov. 14) 1929.

10. Hoskins, R. G., and Sleeper, F. H.: The Thyroid Factor in Dementia Praecox, Am. J. Psychiat. **10**:411 (Nov.) 1930.

thyroid a day can often be tolerated for weeks without marked elevation of oxygen consumption or pulse rate. The question was left open whether the defect was in absorption of the administered thyroid substance or in tissue oxidation. Recently the thyroid studies have been continued by Cohen,[11] who has noted that the low responsivity is evident also when thyroxin is given by vein. His patients have tolerated doses up to 5 mg. daily without showing dangerous reactions.

Similarly, in a preliminary study, Freeman [12] found that the schizophrenic person is less than normally responsive to dinitrophenol, which is a powerful oxidative stimulant.[13]

In previous publications attention has been called to the evidence that the schizophrenic person gives less than a normal stimulatory response to the proteins of his food; i. e., he shows reduction in the so-called specific dynamic action. Fischer [14] has emphasized this defect as a central feature in the schizophrenic psychosis. He reported that the "specific dynamic action" begins to decrease with the onset of the psychosis, to persist at a reduced level as long as the psychosis is active, to increase with clinical improvement of the patient and to become normal when full remission is attained. My colleagues and I have attempted to repeat Fischer's studies, but, because of the rather marked variability in the rates of oxygen consumption as actually recorded, we have not been able either to confirm or to refute Fischer's work. More recently, Freeman [15] has resumed the study, using amino-acetic acid as representing protein food. When amino-acetic acid was given by vein, no significant change in the metabolism was detected, but when it was given by mouth, in doses of 50 Gm., there was an increase in the rate of oxygen consumption, the rectal temperature and in the rate of insensible perspiration. Whether, however, these findings represent a true specific dynamic action has not been certainly determined.

Altogether, the aforementioned evidence seems to indicate with considerable clarity that a trend toward defective oxygen metabolism is a significant feature in the schizophrenic psychosis. Inadequate oxygen assimilation would have an important influence in cutting down available energy and in handicapping the patient in making adaptive adjustments. The more recent data herein recounted have added further support

11. Cohen, L. H.: Unpublished data.

12. Freeman, H.: Unpublished data.

13. Looney, J. M., and Hoskins, R. G.: The Effect of Dinitrophenol on the Metabolism as Seen in Schizophrenic Patients, New England J. Med. **210**:1206 (June 7) 1934.

14. Fischer, S.: Gasstoffwechselveränderungen bei Schizophrenen: Differentialdiagnostische Bedeutung, Klin. Wchnschr. **6**:1987 (Oct. 15) 1927.

15. Freeman, H.: Unpublished data.

to the hypothesis advanced four years ago by Jellinek and me [16] that the schizophrenic patient is a victim of "physiological clumsiness." The factors which contribute to the defective oxygen metabolism seem to reside in part in the mechanisms for oxygen transport but more in the factors in the tissues that regulate the oxygen uptake. In some cases one defect, and in other cases a different defect, appears. In an occasional instance several mechanisms are found to be simultaneously at fault. Whether the defective oxygen metabolism is a fundamental cause of the psychosis or merely a feature in its evolution cannot be determined from the aforementioned evidence. In either case, however, the problem becomes increasingly one of tissue chemistry.

The oxidation processes of the body represent a complex series of interactions in which dextrose is oxidized in a linked series of reactions, passing successively through several organic acid stages with carbon dioxide and water at the end of the series. The defective oxidation in schizophrenia might occur at any stage of the oxidation cycle and might be due to lack of either an enzyme or a coenzyme specific to each stage. Thus, the actual problem breaks down into a variety of subproblems. For their solution it will probably be necessary to trace through the oxidation sequence in schizophrenic tissues, setting up ad hoc experiments on systems which include the substrate, the enzyme, the coenzyme and the hydrogen acceptors in each step. In case of the lactic acid stage, it has recently been reported [17] that an appropriate enzyme can be obtained from pig heart and a coenzyme from yeast and that methylthionine chloride can be used as a hydrogen acceptor. In case of most of the organic acids involved in the chain, however, the paradigmatic component factors in the reactions remain to be discovered.

The next step in the problem as related to schizophrenia is obviously to take up a study of the tissue reactions in the Warburg chamber, with the utilization of specimens obtained at biopsy. There is a possibility, however, that the defective oxidation is due to the presence in the internal milieu of abnormal metabolites which serve as anticatalysts at one stage or another in the oxidation sequence. In that case, it may be possible to detect them, using normal living tissue as the reactive system.

SUMMARY

A brief review is offered of some of the work carried on at the Worcester State Hospital for the past decade which bears on the problem of oxygen metabolism in schizophrenia.

16. Hoskins, R. G., and Jellinek, E. M.: The Schizophrenic Personality with Special Regard to Psychological and Organic Concomitants, A. Research Nerv. & Ment. Dis., Proc. **14**:211, 1933.

17. Green, D. E., and Brosteaux, Jeanne: The Lactic Dehydrogenase of Animal Tissues, Biochem. J. **30**:1489 (Aug.) 1936.

It has been found that the rate of oxygen consumption as determined by the method of Benedict and Roth has a significantly lower range in the schizophrenic than in the normal population when the tests are made under the same environmental conditions. A lower range of blood volumes, when these are referred to the surface areas, has been found in schizophrenic than in normal subjects. The circulatory rate as determined by the cyanide method was found to be only about 80 per cent of the normal rate. Despite the slower circulation, the schizophrenic patient was found to abstract no more oxygen than did the control subject. The glutathione and lactic acid levels of the blood were observed to be fairly independent in the control subjects but to be rather closely related in the schizophrenic group, a fact interpreted as indicating the necessity for dependence on the glutathione as an accessory respiratory mechanism. Schizophrenic persons are commonly less responsive than normal to thyroid and probably less responsive to dinitrophenol and amino-acid.

It is concluded that defective oxygen metabolism is an important feature in the schizophrenic psychosis. The next important step in research on the psychosis will be a study of the tissue chemistry with special relation to the oxidation sequences.

DISCUSSION

DR. JOHN CHORNYAK, Pittsburgh: The work reported by Dr. Hoskins indicates definitely that defective oxygen metabolism is an important feature in the schizophrenic psychosis. I wish to supplement these physiologic and biochemical data by fitting into this emerging picture of the fundamental nature of schizophrenia some morphologic data. I shall cite data based on experimental work on rats, dogs and monkeys, and observations on the structural changes produced in the human brain by oxygen deprivation which are pertinent to the problem of oxygen metabolism in schizophrenia.

The pathogenesis of the changes in the nerve cells is, briefly, twofold. The changes in the neurons are primarily conditioned by their metabolic rate, which, under the stimulating action of decreased oxidation, produces rapid lysis of the cells or slower dechromatinization, with less rapid accumulation of intracellular edema. Secondarily, the changes are due to the functional, and later the structural, changes in the blood vessels. They are of the so-called ischemic type and occur irregularly in foci dependent on the site of the vascular lesion. Both processes are due to oxygen deprivation.

In relation to schizophrenia, I am interested in the first of these two processes. There is a remarkable difference in the same brain in the degree of damage to the nerve cells from oxygen deprivation. The most sensitive cells are those in the supragranular lamina of the cerebral cortex. Even this lamina is not uniformly involved; the cells in the so-called psychoprojection, or association, areas are damaged before the corresponding cells in the projection cortex, and the cells in the second layer, before those in the third. The response of these neurons to the stimulating action of decreased oxygen supply is evidently greater than that of any other group in the central nervous system. After the occurrence of circulatory changes, such as stasis, diapedesis and the proliferative endothelial reaction, there are superimposed the ischemic changes in the nerve cells, which may occur irregularly throughout the cortex, depending on the site of the vascular lesion. The cells that have evolved most recently are those showing the greatest vulnerability.

Without entering into a discussion of the historical and controversial aspect of the neuropathology of schizophrenia, I wish to cite some relatively recent work on the problem: Ariëns Kappers, in a memorial lecture delivered recently before the College of Physicians in Philadelphia, reported on the rarefaction of cells in the supragranular lamina. Hechst and Miskolczy, as cited by von Angyal in the March 1937 issue of the ARCHIVES, showed rarefaction of the cells in the phylogenetically youngest, and specifically human, cerebral portion. In Miskolczy's brain maps illustrating the extension and gravity of the pathologic processes, the inferior part of the parietal lobe is one of the regions most involved. On the basis of the investigations of my colleagues and me, it is precisely the cells in these areas that are most vulnerable to deprivation of oxygen.

DR. W. G. LENNOX: It occurs to me that it would be interesting to subject patients to various tensions of oxygen and see if this alters the clinical state. With epileptic patients one can produce a seizure with a degree of anoxemia which has no effect on the normal person. I am anxious for Dr. Hoskins and his associates to work on the brain itself. Measurements of the constituents in blood taken from peripheral vessels are too far afield. The use of blood from the internal jugular vein would be better. Dr. Thompson, who is here, could contribute his observations on the gaseous content of blood from the internal jugular vein in schizophrenic subjects. In such a desperate condition as schizophrenia, securing stab specimens from the brain and measurements of the respiration and the electrolytic content of the blood seem feasible. The demonstration that sodium and potassium are important in the electrical discharge of nerves and that the metabolism of these minerals is influenced by the adrenal cortex, which itself has important connections with the sympathetic nervous system and the emotions, makes this a fascinating and potentially fruitful field for research.

DR. WILLIAM HUGHES, Providence, R. I.: In aviation, ammonium chloride has been found to be of some value in the utilization of oxygen. Has Dr. Hoskins had experience with it?

DR. R. G. HOSKINS: I recognize that it would be highly desirable to study the susceptibility of schizophrenic patients to reduced oxygen tension. If it is assumed that defective oxidation in the brain cells is an important feature in the psychosis, it is obviously of crucial importance to study fresh brain tissue in the Warburg chamber. For the most part, this would have to be obtained by biopsy. Because of the obvious difficulty in securing such material, it is important that one learn as much as possible about oxygen metabolism of the brain by less direct methods. The suggestion that the acid-base relationship is important in determining oxidative efficiency deserves serious consideration. A few years ago my colleagues and I tried to shift the balance toward the acid side by giving the patients ammonium chloride. No effects on the symptomatology were detected. In our study on the gases of arterial blood the radial artery was utilized. Presumably, however, blood from the radial and that from the carotid artery do not differ materially. No significant difference in the gaseous content of the arterial blood of normal control subjects and that of patients has been detected, but, as stated in the paper, the oxygen-carbon dioxide relationships in the venous blood seem to be significantly different. The problem should be studied further with the use of blood from the jugular vein.

Case Reports

POIKILOTHERMIA WITH HYPOTHALAMIC LESIONS

A Clinicopathologic Study

CHARLES DAVISON, M.D., AND EMANUEL D. FRIEDMAN, M.D., NEW YORK

There are sufficient clinical and experimental observations to indicate that the hypothalamic nuclei play an important rôle in the regulation of body temperature. Although most of these investigations were concerned with the abnormal production of heat (hyperthermia), recently one of us (C. D.) and Selby [1] reported a case of severe hypothermia associated with lesions in the hypothalamus. At the time it was postulated that the extreme subnormal temperature in this case was due to implication of the nuclei tuberis proper and the nuclei of the mamillary bodies. As far as we know, inability to maintain the body temperature (poikilothermia) resulting from hypothalamic lesions in man has not been reported previously in the literature.

REPORT OF A CASE

History.—Baby R. was born on Oct. 21, 1932, by spontaneous delivery, after twenty-seven hours of dry labor. The weight at birth was 6 pounds and 9 ounces (2,977 Gm.). The temperature and pulse at birth were normal. The infant cried poorly, and there was a tendency to cyanosis. On the evening of the day of delivery, clonic movements were noted, and the temperature fell to 95 F. The next day there appeared a generalized petechial eruption, which lasted about four days, and a temperature of 95 F. In order to raise the temperature of the child, it was necessary to use heat in the form of hot-water bags and to place the crib near a steam radiator. Lowering the temperature of the room immediately caused a drop of several degrees in the body temperature. On exposing the infant to examination, the body temperature was lowered to such a degree that it failed to register on an ordinary thermometer (that is, to below 94 F.). This instability continued until the baby's death, twenty-nine days after birth. There was also noted at birth a large swelling over the right parietal bone, which was interpreted as caput succedaneum but which was found to be overriding of the right parietal bone, with depression of the left. Throughout its life the infant was apathetic and unable to nurse at the breast, except on one day. It was fed by bottle but gained little in weight and two weeks after birth weighed only 6 pounds and 14½ ounces (3,388 Gm.). The infant was admitted to the Beth Israel Hospital on Nov. 5, 1932; the physical findings differed little from those already noted. The right eye was closed and the left eye normal. The anterior

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From the Neurological Division, the Beth Israel Hospital, and the Neuropathological Laboratory, the Montefiore Hospital.

1. Davison, C., and Selby, N. E.: Hypothermia in Cases of Hypothalamic Lesions, Arch. Neurol. & Psychiat. **33**:570 (March) 1935.

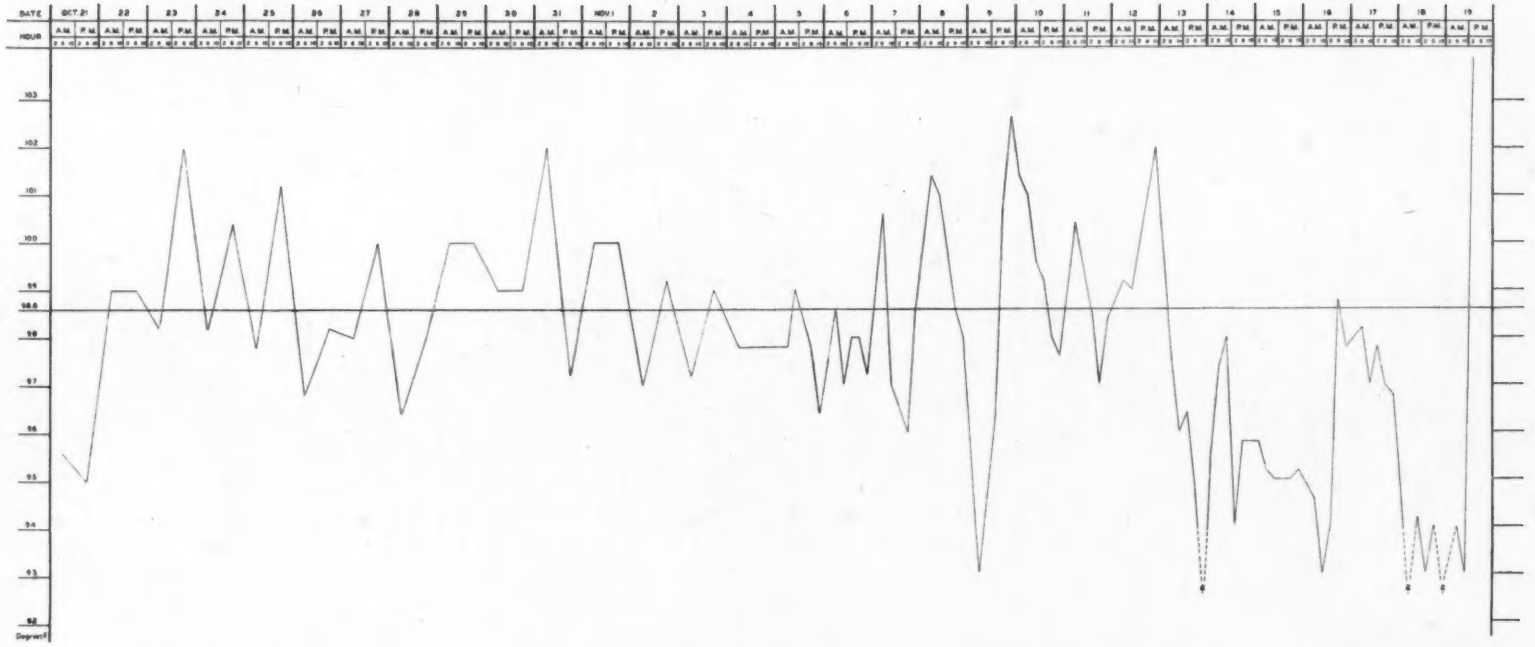

Fig. 1.—Chart showing marked fluctuations in the body temperature, either below or above normal, during the life of the infant.

and posterior fontanels and the lambdoid and sagittal sutures were open. Physical examination gave essentially normal findings except the presence of a large spleen, 2½ fingerbreadths below the costal margin.

Neurologic Examination.—The right palpebral fissure was narrowed. There were gross tremors of all extremities, with athetoid movements of both hands, particularly of the left, and Babinski and Rossolimo signs, ankle clonus and absence of abdominal reflexes bilaterally. The pupils were dilated and did not react to light; the disks and retinas could not be visualized. Throughout the child's stay in the hospital there were marked fluctuations in body temperature, either above or below normal, as indicated in the chart (fig. 1).

Fig. 2.—Anteroposterior view of a ventriculogram, showing enormously dilated ventricles. Notice the air bubbles in various regions.

Laboratory Data.—Spinal tap revealed xanthochromic fluid. The Wassermann reactions of the blood and spinal fluid were negative, and studies of the blood gave normal results. Roentgen examination revealed a large depressed fracture involving a considerable portion of the right frontal bone and an irregular calcareous deposit in the right anterior temporal region. Ventriculography showed enormously dilated ventricles (fig. 2) and calcifications in the region of the caudate nuclei. There was shift of the air in the cranial vault with different positions of the head. In the postero-anterior view the ventricles were no longer visualized. There was no air on the surface on the right side; on the left there was a large collection of air, considerably larger than the combined air shadows in the ventricles. The left side of the brain showed numerous small air bubbles,

which occupied an area corresponding roughly to the anterior parietal and parts of the occipital region. There were no cortical markings.

Course.—The fluctuations in temperature continued. The course was progressively downward, and the infant died on November 19.

Autopsy.—The liver protruded 3 cm. below the costal margin, and the spleen was enlarged. Microscopically, all tissues were normal, except the liver, kidneys and lymph nodes, which showed embryonic blood formations.

Brain: Macroscopic examination: The brain was small and collapsed on removal, owing to the marked hydrocephalus (fig. 3). The convolutional markings were normal from the frontal to the postcentral region. Posterior to this

Fig. 3.—Horizontal section of the brain disclosing marked hydrocephalus and thinning of the temporal, parietal and occipital convolutions.

there was complete absence of convolutional differentiation (fig. 3). The brain was markedly thinned and in several spots appeared only as a layer of pial membrane (fig. 3). These thin spots were symmetrically located in the tip of the temporal lobe and on the lateral, posterior and mesial aspects of the occipital lobe. The agenetic cortex was only 3 or 4 mm. thick (fig. 3), whereas the normal cortex in the frontal region was at least 1.5 cm. in thickness. The region of the floor of the third ventricle was represented only by a layer of pial membrane. On horizontal section the entire ventricular system was markedly dilated (fig. 3); the fornix was absent, and the corpus callosum was represented by an extremely thin layer of tissue. The choroid plexuses appeared normal. In

the region of the anterior parts of the caudate nuclei chalky white substance adhered to the brain. The structures of the midbrain appeared normal. The pineal body was embryonic. The aqueduct of Sylvius was constricted. The cerebellum was small but normal. The fourth ventricle was slightly dilated. A number of areas containing chalky material were seen on the surface; these were not localized to any special point.

Microscopic examination: The meninges of the cortex were slightly thickened and were infiltrated with calcific deposits, compound granular corpuscles and a few endothelial cells; this process was best seen in the island of Reil. Cortical sections showed a normal cyto-architectural arrangement for a child of this age, but the white matter was practically absent. The thin shell of white matter of the cortical convolutions and the zone between the white matter and the sixth

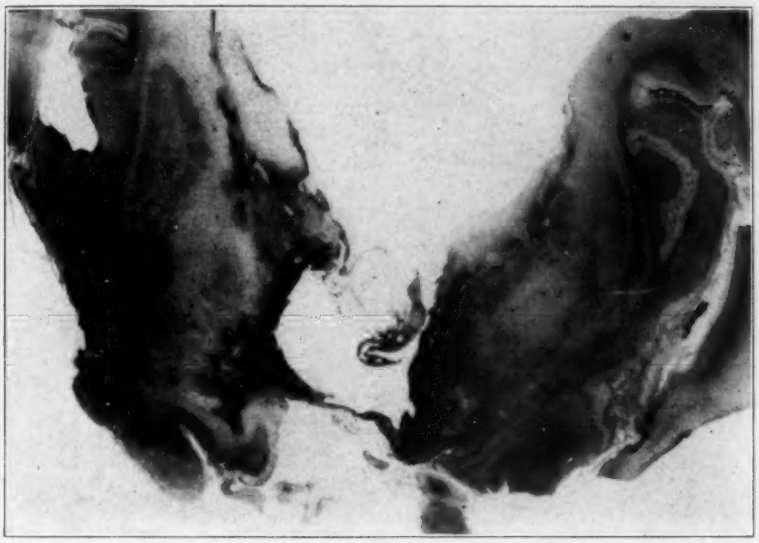

Fig. 4.—Tumor and necrosis destroying most of the hypothalamic nuclei. The third ventricle is lined with calcific deposits. Notice the relative sparing of the basal ganglia and thalamic nuclei.

cortical layer were formed by a zone of microglia cells, proliferating astrocytes and heavy deposits of calcium. The various glia cells were loaded with deposits of calcium. Areas of heterotopia were also noted.

Myelin sheath preparations of sections through the hypothalamus disclosed marked pallor of all the fiber tracts. The internal capsule and the white matter of the globus pallidus and other regions were gone. The third ventricle was dilated (fig. 4). The groups of hypothalamic nuclei could not be identified clearly, as they were infiltrated by calcific deposits and necrotic areas. In cresyl violet preparations the ventricles were lined with deposits of calcium. The entire hypothalamic region stained deeply (fig. 4) and was replaced by tumor and necrotic tissue; it contained calcific deposits, microglia and other glia cells, compound granular corpuscles, neuroblasts, fibroblasts, calcified blood vessels and débris (fig. 5). The perivascular spaces in this area were loaded with deposits of calcium and compound granular corpuscles. In the region of the various hypo-

thalamic nuclei the collections of neuroblasts, medulloblasts and primitive ganglion cells stood out prominently (fig. 6*A* and *B*). Most ganglion cells of the supraoptic nucleus were spared (fig. 7). A few of these nerve cells appeared as shadow cells, and many had lost their normal iron pigment. The ganglion cells of the nucleus paraventricularis, nucleus paramedianus, nucleus reuniens, nucleus mamillo-infundibularis and nucleus mamillaris were destroyed. The mesially grouped

Fig. 5.—Area of necrosis showing débris, calcific deposits, compound granular corpuscles, microglia cells and neuroblasts. Hematoxylin and eosin stain; × 100.

nuclei, especially the nuclei tuberis proper, were most extensively involved. The pathologic process in the hypothalamus extended from the anterior part of the chiasm past the mamillary bodies.

Similar changes were also noted in the region of the optic chiasm, in part of the caudate nuclei and in the pons. A discrete tumor nodule was noted in the pons (fig. 8); it was situated slightly to the left and did not differ histologically from the tumor in the hypothalamic region. There was absence of myelinization of the pontile fibers (fig. 8). Sections below this showed insignificant changes.

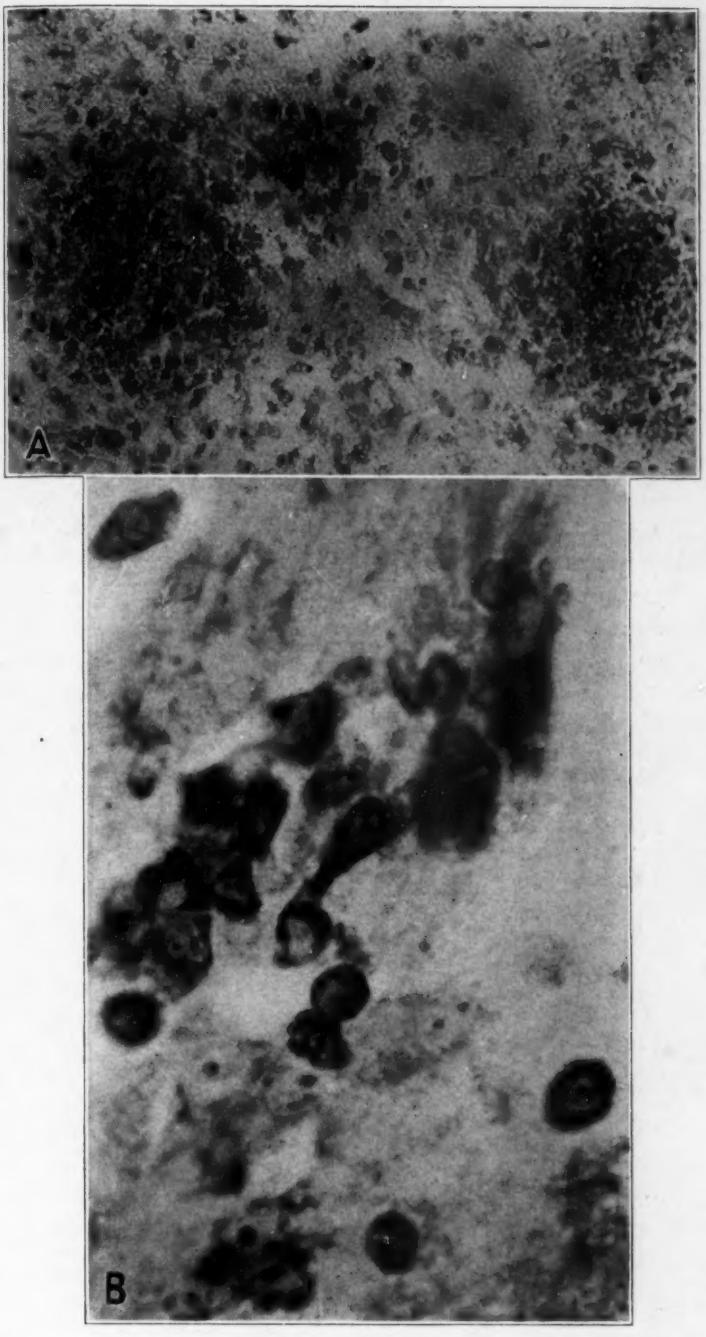

Fig. 6.—(*A*) Collections of neuroblasts and medulloblasts; × 100. (*B*) Neuroblasts from the tumor; × 900. Cresyl violet stain.

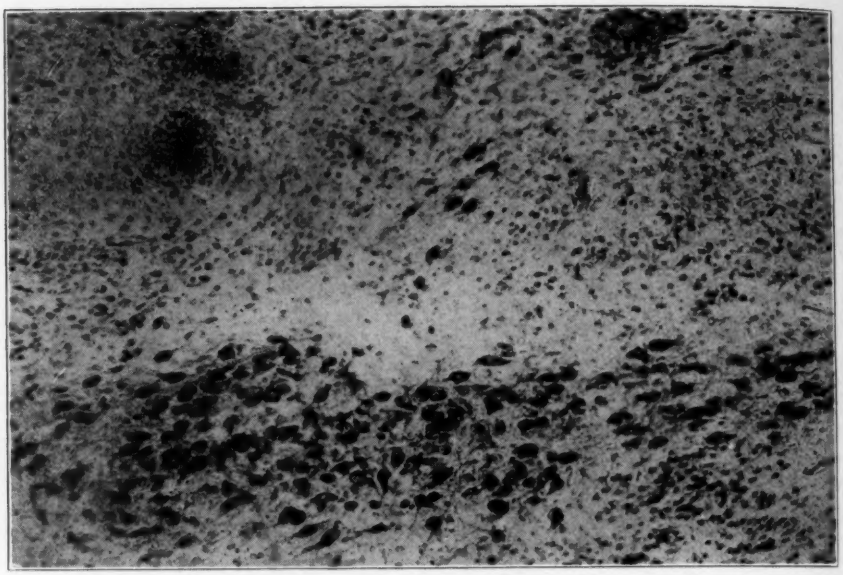

Fig. 7.—Nodules of neuroblasts and areas of destruction in the region of the hypothalamus. Notice that the nucleus supra-opticus is spared. Cresyl violet stain; × 50.

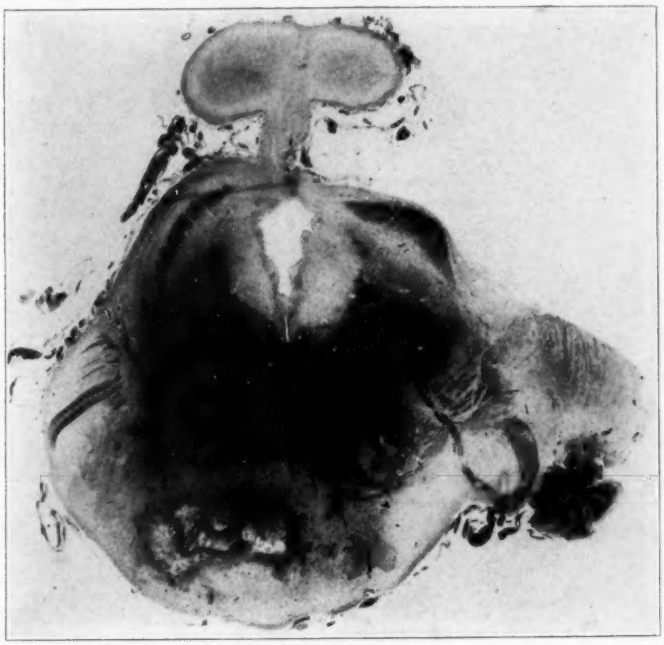

Fig. 8.—Section of the pons, showing the tumor nodule situated in the left side and absence of myelinization of pontile fibers.

COMMENT

This clinical case of poikilothermia and that of hypothermia[1] previously reported are of interest in regard to the influence of the hypothalamus on the regulation of body temperature. It should be emphasized that although the hypothalamic nuclei are the main centers for the control of normal body temperature, there are other regions of the central nervous system which alone or through neural connections with the hypothalamus regulate the normal maintenance of body temperature. Pinkston, Bard and Rioch[2] and others have shown that cats after removal of the cerebral cortex frequently shivered at ordinary temperatures. These observations on animals with a unilateral lesion or with ablation of limited portions of the cortex suggested that cortical control of vasomotor responses to changes in temperature is localized in the contralateral "motor-sensory area." These authors concluded that "several levels of the nervous system, including the cortical, are necessary for normal temperature control." It is unlikely, however, that in our case bilateral involvement of the "motor-sensory area," as a result of the generalized internal hydrocephalus, produced the disturbance in regulation of body temperature. Should the motor and sensory areas play an important rôle in control of temperature, one would expect to notice frequent disturbances in the maintenance of normal temperature in cases of hydrocephalus and other lesions of these structures. Hyperthermia may ocasionally be found, while hypothermia was reported by Stettner[3] in only one instance of hydrocephalus.

An objection which might be advanced in our case is that in newly born children, if artificial heat is not supplied, fluctuations in temperature may occur because of an inadequate temperature-regulating mechanism. The ability to dissipate excess heat by perspiration and increased respiration is also imperfectly developed. For these reasons the temperature in the first few days of life may show wide variations, falling or rising 4 or 5 F. below or above normal. In our case this disturbance in temperature appeared shortly after birth and could not be controlled, in spite of the immediate steps taken to maintain the room temperature between 80 and 90 F. and the use of other artificial methods to keep the infant's body warm.

There is some evidence that the pons and medulla oblongata also contain centers and pathways concerned with control of temperature. Injuries or hemorrhages in the pons or medulla oblongata were observed to be associated with disturbance in the regulation of temperature, showing especially a trend to hyperthermia. The centers in the medulla oblongata, as demonstrated by Beattie, Brow and Long,[4] are probably

2. Pinkston, J. O.; Bard, P., and Rioch, D. McK.: The Responses to Changes in Environmental Temperature After Removal of Portions of the Forebrain, Am. J. Physiol. **109**:515, 1934.

3. Stettner, cited by Gagel, O.: Symptomatologie der Erkrankungen des Hypothalamus, in Bumke, O., and Foerster, O.: Handbuch der Neurologie, Berlin, Julius Springer, 1936, vol. 5, pt. 5, p. 482.

4. Beattie, J.; Brow, G. R., and Long, C. N. H.: Physiological and Anatomical Evidence of the Existence of Nerve Tracts Connecting the Hypothalamus with Spinal Sympathetic Centers, Proc. Roy. Soc., London s.B **106**:253 (May 3) 1930.

in intimate relationship with the hypothalamus, which is the main center for the regulation of normal temperature. It would be expected that lesions anywhere along this descending tract may cause disturbances in control of temperature.

The mesial, bilateral and symmetrical lesions in our case destroyed the rostral and the posterior part of the lateral portion of the hypothalamus. These lesions corresponded to those observed by Ranson and Ingram[5] in monkeys and by Frazier, Alpers and Lewy[6] in cats. The bilateral mesially and laterally placed lesions destroying the floor of the third ventricle and the lateral walls of the hypothalamic nuclei probably accounted for complete disturbance in the temperature-regulating mechanism and the resulting poikilothermia in this case. As already noted by Frazier and his co-workers, laterally placed lesions cause only transitory and fleeting disturbances in regulation of temperature. The nuclei supra-optici, which probably control sugar and water metabolism, were spared in our case to a certain degree. This possibly accounts for the absence of polyuria and glycosuria. It should be emphasized, however, that owing to obvious obstacles the water and sugar metabolism were not adequately studied in this instance.

SUMMARY

The constant fluctuations in the temperature of the body in our patient consisted of hyperthermia and hypothermia and tended to approximate the environmental temperature. In addition to generalized internal hydrocephalus, most of the hypothalamic nuclei, especially the mesial group, were destroyed by an infiltrating neuroblastoma. The poikilothermia in this instance was probably caused by the lesion in the mesial group of hypothalamic nuclei.

DISCUSSION

DR. E. D. FRIEDMAN: We have presented evidence of the importance of the hypothalamic zone in the regulation of body temperature. It had long been known that puncture of the stritum (*Wärmestick*, of the Germans) gives rise to fever. Aronsohn and Sachs stated that the caudate nucleus contains a center for the regulation of body temperature. Eisenstaat and Streerath asserted that the thalamus is the center presiding over heat regulation. Ernest Sachs, however, expressed the belief that the basal ganglia play no part in this mechanism.

Jacoby and Rohmer found that the introduction of mercury into the ventricles of the brain, especially into the infundibular region, gives rise to severe and persistent hyperthermia. They found that only injury or inflammation of the ventricular wall causes fever. Isenschmidt and Krehl and Isenschmidt and Schnitzler localized the center in the tuber cinereum. Greving postulated the presence of centers for fever in the wall of the third ventricle, in relation to the centers for perspiration and vasomotor control. Brumann used the thermo-electric method and found that injury to the ventricular wall is the important factor giving rise to hyperthemia. Strauss and Globus reported three cases of cerebral neoplasm in which fever was a prominent symptom. In all lesions were observed in or near the hypothalamic zone.

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5. Ranson, S. W., and Ingram, W. R.: Hypothalamus and Regulation of Body Temperature, Proc. Soc. Exper. Biol. & Med. **32**:1439, 1935.

6. Frazier, C. H.; Alpers, B. J., and Lewy, F. H.: The Anatomical Localization of the Hypothalamic Centre for the Regulation of Temperature, Brain **59**:122, 1936.

Cushing, in his recent Lister Memorial lecture, reported hyperthermia in children following the complete emptying of the ventricular system and also in the case of a large suprasellar meningioma in which there was a chiasmal syndrome. In the latter there was a postoperative rise of temperature, which continued for ten days, without coincident leukocytosis or evidence of infection. Bazett, Alpers and Erb found that in cats the area in the walls and floor of the third ventricle is essential for the regulation of temperature. Alpers also studied 2 cases of tumor in the pituitary zone in which death followed severe hyperthermia and loss of temperature control. In these cases the lesions were in the floor of the third ventricle.

I also had occasion to report a case of tumor of the brain in which there was persistent and unexplained hyperthermia. In this case there were two neoplastic lesions, one involving the left temporal lobe, which gave rise to mental symptoms and aphasia, and another involving the right thalamus and hypothalamic zone, which apparently was responsible for the persistent and otherwise unexplained hyperthermia. Similarly, abortive encephalitis may appear in the guise of unexplained fever. In such cases the tuber cinereum is frequently involved and is probably the source of the disturbance in temperature regulation. Only with the advent of the subsequent parkinsonism can the diagnosis be made in retrospect.

Lewy recently reported the results of experimental work in cats. He found that bilateral mesially placed lesions in the floor of the third ventricle, produced by the Horsley-Clarke apparatus, give rise to complete loss of temperature control. It was his belief that the vital area for the regulation of temperature in the hypothalamus is in the floor of the third ventricle, corresponding to the substantia grisea in man. Davison and Selby recently reported the incidence of hypothermia in the case of an angioma situated in the floor of the third ventricle, which destroyed a number of nuclei in the hypothalamic zone.

We have presented a further link in the chain of evidence which points to the hypothalamic area as the center for the regulation of body heat.

DEVELOPMENT OF APPARENT UNCONSCIOUSNESS DURING HYPNOTIC RELIVING OF A TRAUMATIC EXPERIENCE

MILTON H. ERICKSON, M.D., ELOISE, MICH.

A general experimental project, to be reported later in its entirety, was undertaken to investigate the possibility of exploration by means of hypnosis of the psychic development of a patient recently recovered from an acute psychotic episode of a schizophrenic reaction type.

The method employed consisted of an attempt to have him relive his past life as completely as possible in a special state of hypnosis.

METHOD

The experimental procedure consisted of training the patient to enter profound somnambulistic hypnotic trances, during which, by means of a series of hypnotic suggestions, he was disoriented completely and then reoriented to an earlier period of his life. When thus reoriented, by the employment of carefully worded systematic suggestions and questions, he was induced to relive past events in a chronologically progressive fashion, describing them in detail to the experimenter as if they were in the course of actual development in the immediate present. An attending stenographer recorded in full the entire course of the experimental events, including the descriptive material. In every instance for which relatively adequate data were available from sources other than the patient himself, it was found that events of the distant past were relived and recounted by the patient with remarkable vividness, and with richness and accuracy of detail.

In this connection, mention should be made of the fact that neither detailed questioning in the normal waking state nor instruction to recall fully these past events in a state of ordinary deep hypnosis served to secure the same degree of accuracy and amount of detail as did the procedure of reorientation. Furthermore, even after the patient had relived an experience while reoriented to that period of his life, such completeness of recall could not be secured without resort to posthypnotic suggestions worded in such fashion as to bridge the temporal gap between the actual present of the experimental situation and the chronological period to which the patient had been reoriented. The following example illustrates such posthypnotic suggestion: "This thing that has just happened to you and which you have told me about is important. You are to remember it fully and completely for the rest of your life, so that ten, or even twenty, years from now, it will be as fresh in your mind as it is now."

EXPERIMENTAL RESULTS

Study of the experimental findings disclosed an incident of peculiar interest, illustrative in an unusual fashion of psychosomatic interrelationships. This incident concerned the development of what appeared to be a state of unconsciousness as the patient relived the experience of a homicidal assault which had occurred two years previously, when he was 17 years old. All previous information concerning this assault consisted of the statement by the patient that he had been "taken

for a ride" and beaten so badly that hospitalization had been necessary. He seemed to have complete amnesia for all informative details of this experience, including even the name of the hospital. Extensive and persistent questioning in the ordinary deep hypnotic trance, as well as in the normal waking state, secured only unimportant items, despite the fact that he seemed to be cooperating to the limit of his ability.

When the day of this event was reached in the hypnotic reliving of his past life, the patient expressed his fears over his employment as a police informer, portraying vividly intense anxiety concerning threatened criminal vengeance, and his entire behavior and appearance were suggestive of a most harried state of mind. When the hour of 4 p. m. was reached in his reexperiencing the events of this day, he relived, with marked intensity of feeling, the scene of his being ordered into an automobile by two men whom he knew to be criminal characters and his fearful behavior during the course of a long drive, during which he pleaded piteously with his abductors in a terrified fashion. Finally, he reenacted his forced acceptance of a bottle of pop from the criminals, fearfully and hesitantly drinking from an imaginary bottle. As he swallowed, he grimaced, mumbled that it tasted bitter, asked if it was poisoned and dodged and cowered as if evading a blow. His entire appearance continued to denote intense terror. Shortly after completing the act of drinking he belched and suddenly looked bewildered. His pupils, which previously had been fluctuating constantly in size, became widely dilated, and fine lateral nystagmus developed. He then rubbed his eyes, complained that he could not see plainly, said that everything was getting dark and that he was dizzy and began shaking his head as if to throw off something or to rouse himself. Questioning by the experimenter elicited the information that the patient felt himself becoming sleepy. It was noted that his speech, previously clear, was now thick and indistinct and that his appearance had changed from that of terror to that of somnolence.

At this time the patient was sitting on a couch, and every few seconds the experimenter had been testing him for the presence of catalepsy as an index of his continuance in the hypnotic state. After about two minutes of decreasing activity, during which the patient shook his head more and more slowly and mumbled with increasing inarticulateness, his eyes closed, despite his apparent effort to keep them open. Suddenly he gave a short, gasping grunt and collapsed, sprawling inanimately over the couch. Immediate examination by the experimenter disclosed complete loss of hypnotic rapport, with absence of the catalepsy which hitherto had been consistently present. Physically, there were sagging of the lower jaw and marked atony of the muscles of the legs and arms. Also, the patellar and pupillary reflexes, which are consistently present during hypnotic states, were absent. The respiration and pulse, which had been greatly increased during the state of terror, had decreased somewhat during that of somnolence. Now they were found to be markedly diminished in rate and so weak and faint as to be barely perceptible. In brief, the patient presented every appearance of being unconscious. However, before the blood pressure and accurate counts of the pulse and respiration could be taken, the patient seemed to be recovering. He stirred slightly and moaned, and catalepsy returned slowly. Shortly he opened his eyes and, after staring vacantly around, weakly closed them again. It was noted that the pupils were still widely dilated, that fine nystagmus was present and that the eyes were not focused. The patient licked his lips repeatedly, moaned for water and weakly rubbed his forehead, grimacing with pain as he did so. He paid no attention to the experimenter's insistent questions, "What's the matter? What's happening?" except to say, "It's dark, dark." This was followed by a

second collapse, of slower onset than the first but apparently of the same character, with the same physical findings except that the respiration was deep and labored while the pulse was slow and firm. Repeated attempts were made by the experimenter to arouse the patient, but he remained unresponsive for several minutes. Finally, catalepsy returned, and the patient opened his eyes and stared about unseeingly. Nystagmus was absent, and the pupils were somewhat dilated but responsive to light. He twisted his head about, moaned and rubbed his neck as if it were painful, rubbed his forehead gently, grimacing as if with pain and shivered constantly. Again, he licked his lips repeatedly and kept moaning for water. No response was made to the experimenter's insistent questioning except the monosyllables "light" and "woods." Now and then he put his hands to his ears, rubbed them feebly and mumbled, "buzzing."

Soon the patient seemed to recover to a considerable degree, and he again became fairly responsive to the experimenter's inquiries, which concerned the events which he was reliving. There followed a relatively inadequate account, as compared with his initial communicativeness, of lying in a ditch alongside a road through a woods, of being cold, wet and uncomfortable and of suffering from intense thirst, roaring in the ears, headache and a painful, bleeding wound on his forehead, from which he went through the act of wiping blood in a gingerly fashion. He also declared that it seemed to be morning.

From then, he recounted in a fragmentary fashion the experience of being picked up by some men and taken to a hospital. The reliving of the next two days was also disjointed and inadequate, but that of subsequent events was complete, during the course of which the name of the hospital was obtained.

The total time required by the patient to relive this entire experience, which had actually extended over a period of two and one-half days, was slightly more than four hours.

Later, inquiry was made at the hospital named by the patient, and the information was obtained that on the morning of the day specified by him he had been found lying in a confused, semiconscious state in a ditch beside a road leading through a woods, suffering from exposure and a contused laceration of the forehead, and that he had seemed not to recover full consciousness for nearly two days. In addition, inquiries made of the police force for which he presumably had acted as informer verified his account of such employment and served to identify one of the criminals whom he had described as a well known police character having a record of being involved in several homicides and as one on whom the patient had informed. Also, the police records disclosed that the patient had made his usual morning report on the day of the assault but had failed to make his evening report and had not been heard from since.

The entire experimental project was interrupted by external circumstances for more than a year. On resumption, it was repeated in its entirety, including the incident already reported. The records obtained were compared with those of the first investigation and were found to be essentially identical, including all the findings contained in this report. The same descriptive details, the same sequences, the same physical manifestations and even the same fragmentary utterances and gaps in the reexperiencing of the events were found. About five months later, in an endeavor to check certain aspects of the major project, the experimenter again had the patient repeat this event, among others. Again, the record obtained was identical with that of the first and second investigations, and the time required for each repetition ranged from three to four hours.

After each experimental session in which this experience was relived, the patient awakened from the hypnotic state with complete and persistent amnesia for

everything that had taken place during the trance. However, he complained bitterly in each instance of severe headache, overwhelming fatigue and weakness and extreme general discomfort, and he was tremulous physically and unstable emotionally. All this he attributed to the hypnosis, although he readily admitted that previous hypnotic work had left no after-effects. In addition, he became antagonistic and hostile toward the experimenter and the idea of further hypnotic work, and special effort, in one instance extending over a month, was necessary to secure continued cooperation.

COMMENT

One of the first considerations in determining the significance of the experimental findings is the validity of the entire investigational procedure. In this regard the reports in the literature disclose that hypnosis can be employed to arouse dormant associations and to recover amnesic material otherwise inaccessible [1] and that it often makes possible an exceedingly vivid and complete recollection of apparently totally forgotten events. Furthermore, recent experimental work by Platonov and Prikhodivny,[2] among others, has indicated that regression in a hynotic state to an earlier period of life is possible, with the reestablishment of its corresponding patterns of behavior uninfluenced by subsequently acquired skills. Other experimental work demonstrates the possibility of producing in the hypnotic state significant personality-situation changes of an objectively measurable character.[3] In the light of these facts, the practicability and validity of the major project as an experimental method become more readily apparent and serve to suggest the reliability of the findings reported here. In addition, there is the confirmation from the hospital where the patient was treated of the facts of his injury and of his confused mental state, which he had duplicated in the experimental situation. The hospital report also served to indicate the possibility, apart from emotional considerations, of a traumatic basis for the general amnesia manifested by the patient for the original experience in the normal waking state and in the simple deep hypnotic trance. Additional confirmation of the reliability of the experimental findings may be found in the identity of the results obtained on repetitions a year and nearly a year and a half later. Such identity suggests both the intrinsic completeness and the credibility of the data.

The possibility of reliving past experiences as a dynamic process is becoming increasingly recognized, and the validity of the phenomenon has been repeatedly demonstrated in both psychiatric and psychoanalytic experience. Perhaps the best example that may be taken from normal life to illustrate the type of findings obtained in this experiment is the relatively common occurrence of the vivid dreaming of a long past event as a current experience. In such dreams often no modifications may be found of the dream responses and behavior which should derive from

1. Erickson, M. H.: The Investigation of a Specific Amnesia, Brit. J. M. Psychol. **13**:143-150, 1933.

2. Platonov, K. I., and Prikhodivny, E. A.: Objective Proof of Experimental Changes of Personality, Psikhoterapia, 1930, pp. 191-203.

3. Huston, P. E.; Shakow, D., and Erickson, M. H.: A Study of Hypnotically Induced Complexes by Means of the Luria Technique, J. Gen. Psychol. **11**:65-97, 1934. Erickson, M. H.: A Study of an Experimental Neurosis Hypnotically Induced in a Case of Ejaculatio Praecox, Brit. J. M. Psychol. **15**:34-50, 1935.

the dreamer's experiences subsequent to the original dreamed-of occurrence, and this despite the fact that the course of the dreamer's life may have been such as to modify or to change completely his capacity to respond in the fashion depicted in the dream. Thus, the adult may dream vividly of being a child in all respects, without the dream responses and behavior reflecting the maturity of his actual status. Such a dream, however, is a spontaneous occurrence; thus it differs from the patient's experience in this investigation, which was the outcome of deliberate experimentation.

The reliving of this patient's experience did not take place in the usual sense in which it is observed in psychiatric and psychoanalytic practice, since it occurred at a "subconscious" level in a peculiar state of hypnosis which precluded any subsequent conscious recollection and since it involved an experience for which the patient had and continued to have essentially total amnesia.

The regression to the earlier period of life at which this experience originally occurred, occasioned by the hypnotic suggestions for reorientation, apparently functioned in such fashion that all experiences subsequent to that event, including even development of the amnesia, were eliminated by hypnotic dissociation from the patterns of response which were manifested in the experimental situation. Thereby, revival of the experience with its associated responses was permitted as if it were in the course of actual development. Once this process had been initiated by the evocation of readily accessible memories, the recovery of each item functioned in itself as an aid in recovering additional material in its original chronological order, thus constituting a continuous progression to completion of sequential activity. Hence, there would be aroused in proper order and relationship the concomitant psychic and somatic activities with their corresponding alterations and adjustments of the mental and physical states, the entire process being directed by the originally established patterns of response.

The apparent state of unconsciousness developed in the patient raises immediately the question of psychosomatic interrelationships. It is unfortunate that the exigencies of the experimental situation, including the emphasis on the project as a whole, resulted in failure to secure more adequate data concerning his physical state. However, every item of such information which was secured, including the startling clinical effect of the patient's appearance, strongly suggests that he was actually unconscious. More particularly is this indicated by the absence of the pupillary and patellar reflexes, the changes in pulse and respiration and the loss of muscular tonus, all of which are unaffected by the hypnotic state, except muscular tonus, which may be slightly increased.[4] Further confirmation of the possibility that actual unconsciousness was produced may be found in the familiar phenomenon of a faint produced by purely psychic stimuli and, more closely parallel with this experiment, in the faint that has been known to result from a terrifying dream.

Likewise, the after-effects of which the patient complained in each instance after the reliving of his experience are highly suggestive that the processes involved had been of such character as to produce definite somatic and physiologic changes which were not limited to the experi-

4. Bass, M. J.: Differentiation of the Hypnotic Trance from Normal Sleep, J. Exper. Psychol. **14**:382-399, 1931.

mental hypnotic state but persisted into the following waking condition. Further evidence for the possibility that marked changes in the functioning of the body can result from psychic factors may be found in a report made before the American Psychiatric Association in May 1936 on the experimental production of deafness in the hypnotic state.[5]

The temporal abridgment in the experimental situation of the probable period of unconsciousness signifies possibly a qualitative as well as a quantitative difference, to be attributed to the fact that the experimental state of unconsciousness arose from mental and physical states developing in response to internal stimuli, in contrast to the external factors involved in the original experience.

A question may be raised concerning the reason that the patient, on becoming unconscious in the trance state and thus disrupting the hypnotic condition, did not recover consciousness in the normal waking state. Aside from the fact that the entire process was conditioned by hypnosis, the parallel phenomenon is frequently observed of recovery from sudden traumatically induced unconsciousness marked by reorientation to the situation immediately preceding the trauma.

In conclusion, mention may be made of the clinical psychiatric effects of the hypnotic reliving of the patient's traumatic experience. Unfortunately, a complete study of these changes was not made at the time, but certain clinically significant alterations of behavior occurred. After the first hypnotic reliving, despite the fact that no apparent change in his conscious amnesia was detected, the patient showed complete loss of his phobic reactions to visiting the city where he had been a police informer, although, as was learned on questioning, he did not revisit his former haunts, rationalizing this failure with a casual explanation of lack of time. After the second and third experiences in reliving, no apparent trace of any of his fears remained, and he revisited his former haunts with every evidence of pleasure. Some months later, during a casual conversation, he reminded me that he had once told of being taken for a ride without being able to remember many of the details. He then added that he had recalled more of that experience "a few days ago," stating that "Whitey and another guy picked me up on Washington Street about 4 o'clock one afternoon and took me for a ride. They drugged me, conked me and shoved me in a hospital—I think it was in Providence—they were after me for squealing on them. They said they'd get me, but they didn't." This was all he seemed to recall, and he told it casually, with no manifestation of the affective strain and tension previously much in evidence. The marked contrast between his original fearful, hesitant manner of telling what he remembered and this casual, unconcerned elaboration of the story suggests that a definite emotional catharsis had resulted from the hypnotic procedure, even though the entire process had occurred at a level below conscious awareness.

CONCLUSIONS

The specific conclusion to be derived from this report may be stated as follows:

Significant psychosomatic changes culminating in the development of and recovery from an apparently definite state of unconsciousness

5. Erickson, M. H.: A Study of Hypnotic Deafness by Means of a Conditioned Response, to be published.

were produced in a patient during the hypnotic reliving of an amnesic traumatic experience.

More general conclusions are: 1. Hypnosis can be employed to produce significant personality-situation changes, as evidenced by the definite psychic and somatic effects produced by the reorientation to and the reliving of a past experience as a current process.

2. The procedure of hypnotic reorientation to a past event makes possible the reliving of that experience as if in the course of the actual original development, thus excluding the modifying effects of the perspective and the secondary emotional reactions which obtain in the normal waking state and permitting revival of the experience in a more sequential order and in greater detail than is possible in the normal state.

3. Amnesia, even when associated in origin with the physical conditions of trauma to the head and possible narcosis, need not preclude recovery of the major memory images.

Technical and Occasional Notes

DEVICE FOR CONTROLLED FARADIC STIMULATION

FREDERICK A. FENDER, M.D.,* AND R. R. NEWELL, M.D., SAN FRANCISCO

In both the laboratory and the operating room we have felt the lack of a simple, accurately controlled device for faradic stimulation of the cortex. Without discussing the apparatus designed and used for this purpose, it may be said that most have one or both of the following

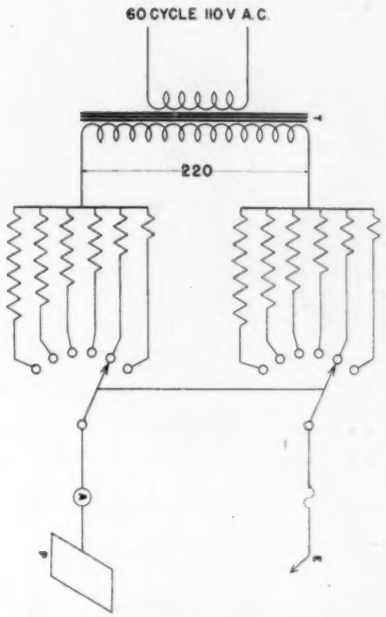

Fig. 1.—Circuit for controlled faradic stimulation. The high value of potential, controlled by correspondingly large resistors, fixes the value of the current, independent of small changes in tissue resistance.

faults: They are too complex to be used in the operating room by the "workaday" surgeon, or the currents they deliver for stimulation cannot be controlled easily enough. In the device described here, we sought graded, predetermined currents at a suitable frequency and in a satisfactory wave form.

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The work was financed by grants from the Committee on Scientific Research of the American Medical Association.

Commercial 110 volt, 60 cycle alternating current is used to supply power. A relatively high voltage (220 volts) is delivered to the stimulating circuit. The current that may flow, however, is limited by graduated resistances, selected by a switch. These resistances are of relatively high order, as compared with the resistance of the tissue pathway. Hence, ordinary variations in resistance in the tissue pathway leave the currents flowing practically unchanged.

In application (fig. 1) a transformer (*T*) is used to increase the voltage supply from 110 to 220 volts. Six pairs of resistors, supplying totals of 440,000, 220,000, 73,000, 55,000 and 44,000 ohms, are placed in the two secondary leads. A two gang, dial type switch is used for choosing any pair of these. Depending on the position of this switch,

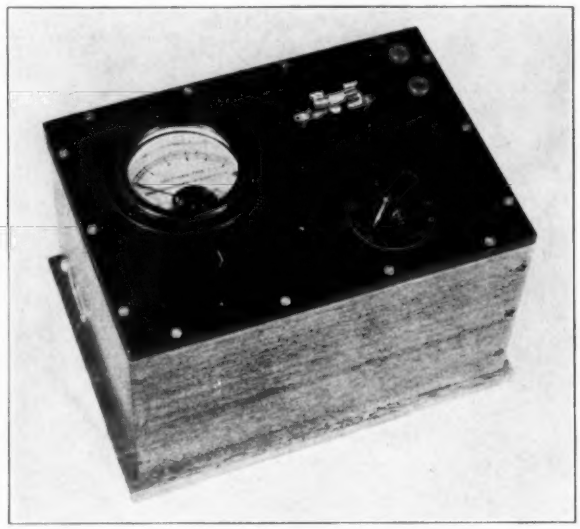

Fig. 2.—Photograph of the apparatus in its box.

the current that flows when the stimulating electrode touches the cortex is 0.5, 1, 2, 3, 4 or 5 milliamperes. A copper oxide rectifying type of milliammeter is placed in one arm of the secondary circuit to enable the operator to check and record results, and a 15 milliampere fuse is included to protect the apparatus and tissues. The indifferent electrode (*P*) is a lead foil plate with an area of about 36 square inches (200 sq. cm.), and the active electrode (*E*) is a 20 gage silver wire in an appropriate insulating handle. Tests have shown that the capacitance of the device is not great enough to allow sufficient electricity to be stored to produce a contraction or to give a deflection of the milliammeter. It is recommended that other electrical devices be disconnected while stimulation is in progress.

The device as assembled in our laboratory is shown in figure 2. Parts may be purchased in radio supply stores, at a cost of about $20.

ADAPTATION OF THE ORIGINAL WEIGERT TECHNIC FOR STAINING MYELIN SHEATHS IN FORMALDEHYDE-PYROXYLIN MATERIAL

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The progress of neuropathology has been seriously hampered by the fact that the demonstration of various tissue elements requires not only a variety of staining methods but several different types of fixation and embedding. This involves the expenditure of much time, expense and material and renders difficult the comparison of different structures in the same lesion. The importance of being able to stain myelin sheaths, axis-cylinders, glia fibrils and cells, respectively, in adjacent sections from the same block can scarcely be appreciated by any one who has limited himself to the "classic" methods of studying these structures.

A full range of stains is available for use with frozen sections of material fixed in a solution of formaldehyde and, of course, certain stains can be used only with frozen sections, such as the stains for fat and certain silver stains.[1] It is difficult to obtain perfect sections of ideal thinness, however, and the stains for myelin of the Spielmeyer type with the use of an iron mordant are open to criticism. Frozen sections for special purposes may be taken without appreciable damage from blocks of tissue fixed in a solution of formaldehyde to be embedded later in pyroxylin. Brief immersion in dilute ammonia water to remove the formaldehyde appears to aid staining.

Tissue fixed in Müller's fluid and embedded in pyroxylin may be used for the classic Weigert myelin stain, glia fibril stains, the Marchi stain, thionin or other cell stains, the Mallory connective tissue and phosphotungstic acid-hematoxylin stains and the Masson stain. Fixation in Müller's fluid is time consuming, however. It is difficult to cut thin sections, and no satisfactory stains for axis-cylinders are available at present.

The use of paraffin as an embedding material has the advantage of speed and convenience and permits the preparation of extremely thin sections. It gives its best results after fixation in Zenker's solution with the ordinary connective tissue and nuclear stains. Unless the material is freshly fixed, cells are likely to be distorted, and there are no thor-

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From the Department of Neurology, the Harvard University Medical School and the Neurological Unit, the Boston City Hospital.

1. Spielmeyer, W.: Technik der mikroskopischen Untersuchung des Nervensystems, ed. 4, Berlin, Julius Springer, 1930.

oughly satisfactory myelin stains which can be used with it.[1] In our experience, the Mallory connective tissue stain gives a better idea of the state of the myelin than does the Morgan stain and is a satisfactory stain for general purposes.

Tissue embedded in pyroxylin after a brief fixation in formaldehyde may be used for a great variety of stains, and sections may be cut as thin as 10 microns if the knife has been properly sharpened, preferably on an automatic hone.[2] We recommend for orientation the use of the Mallory connective tissue method without mordanting in a bichromate; it shows the presence or absence of myelin, axis-cylinders and glial fibrosis, as well as differentiating the connective tissue structures. Cells may be adequately stained with cresyl violet after prolonged soaking in alcohol [1] or, better, with gallocyanine.[3] Axis-cylinders may be stained by the Davenport method,[4] and such preparations compare with those prepared by the original Bielschowsky technic. Glia fibrils may be stained by the phosphotungstic acid or the Anderson [5] or Holzer [1] technic. Alterations in the blood vessels and meninges are beautifully shown by the Masson stain,[6] which may be used also as a substitute for the Alzheimer-Mann method. The Weil-Davenport silver stain for glia may well replace the Cajal method,[7] and silver stains for oligodendroglia and microglia are also available.[8]

The obvious advantages of material fixed in formaldehyde and embedded in pyroxylin has led to the introduction of various stains for myelin sheaths for use with it, of which the Loyez stain [1] has been the most successful in our hands. It is not, however, as specific as the original Weigert method. Cell nuclei are usually stained to some extent and so may be axis-cylinders and glia fibrils (figure, *A* and *B*). We have had no success with the methods described by Flesch and by Gudden.[9] The following method gives results in every way comparable to those obtained by the original Weigert procedure.

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2. Putnam, T. J.: Simple Automatic Sharpener for Microtome Knives, J. Lab. & Clin. Med. **19**:199, 1933.

3. Einarson, L.: A Method for Progressive Selective Staining for Nissl and Nuclear Substance in Nerve Cells, Am. J. Path. **8**:295, 1932.

4. Davenport, H.: Staining Nerve Fibers in Mounted Sections with Alcoholic Silver Nitrate Solution, Arch. Neurol. & Psychiat. **24**:690, 1930.

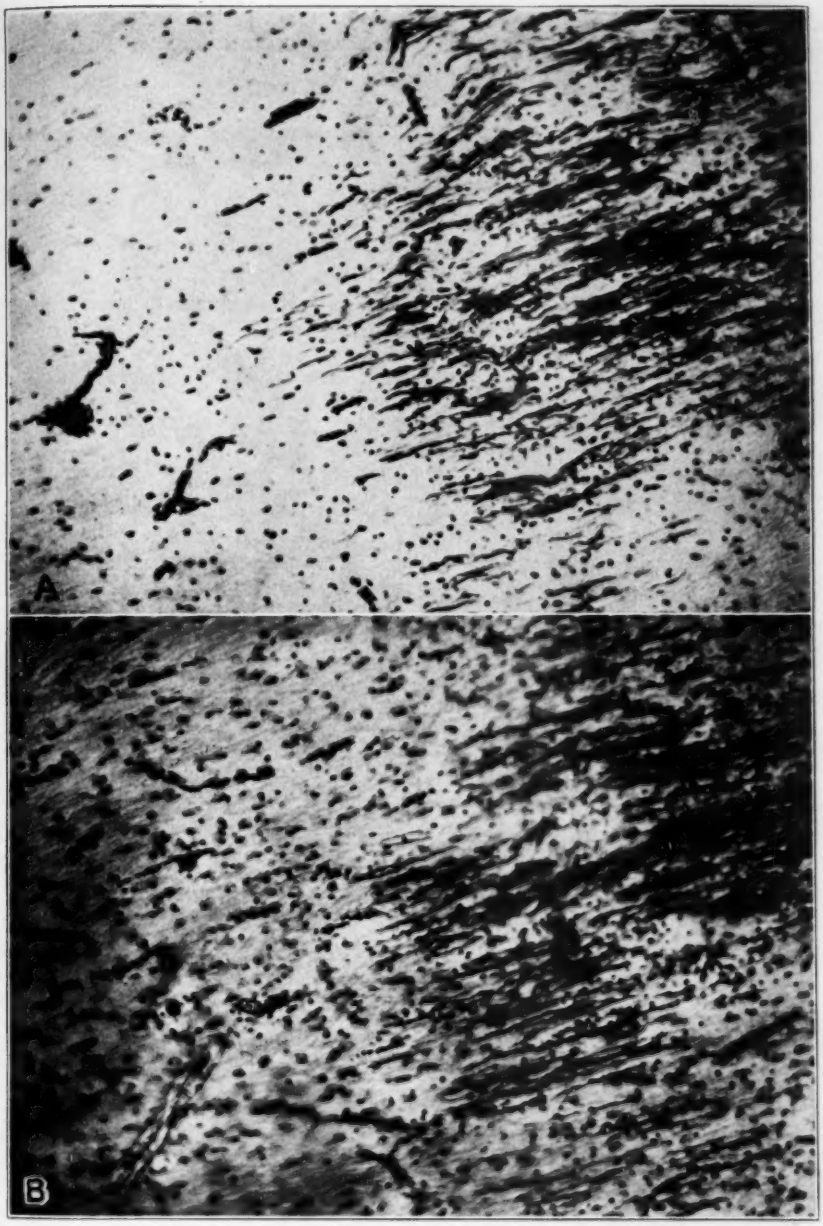
5. Anderson, J.: How to Stain the Nervous System, Edinburgh, E. & S. Livingstone, 1929.

6. Masson, P.: Some Histologic Methods: Trichrome Stainings and Their Preliminary Technique, J. Tech. Methods **12**:75, 1929.

7. Weil, A., and Davenport, H.: Eine Methode zur Silberimpraegnierung von Gliomen, Ztschr. f. d. ges. Neurol. u. Psychiat. **126**:796, 1930.

8. Weil, A., and Davenport, H.: Staining of Oligodendroglia and Microglia in Celloidin Sections, Arch. Neurol. & Psychiat. **30**:175 (July) 1933.

9. Gatenby, J. B., and Cowdry, E. V.: Microtomist's Vade-Mecum, ed. 9, Philadelphia, P. Blakiston's Son & Co., 1928, p. 657.



Photomicrographs (low power enlargement) of sections in a case of multiple sclerosis. *A* is a section showing a myelin "island" at the edge of a plaque, stained by the proposed modification of the Weigert stain, with sharp differentiation. *B* is an adjacent section from the same block, stained by the Loyez iron mordant method. The results may be compared with the differentiation in *A*.

MODIFICATION OF THE WEIGERT-PAL METHOD OF STAINING THE MYELIN SHEATH FOR MATERIAL FIXED IN FORMALDEHYDE AND EMBEDDED IN PYROXYLIN

1. Cut sections at from 25 to 30 microns.

2. Dehydrate in graded alcohols.

3. Remove the pyroxylin from the sections with any of the usual solvents, i. e., equal parts of absolute alcohol and ether, methyl alcohol or acetone. It is important that the pyroxylin should be entirely removed. If not, it interferes with the subsequent mordanting and results in a "patchy" stain. By leaving the sections overnight in methyl alcohol and changing this solvent one or two times, the pyroxylin is entirely dissolved.

4. From the methyl alcohol, or other solvent used, carry the sections through absolute alcohol, 95 per cent alcohol, and so on, to distilled water.

5. Mordant sections for from twenty-four to forty-eight hours at 37 C. in Weigert's primary mordant (*Schnellbeize*).

6. Wash in distilled water and stain from twelve to twenty-four hours at 37 C. in the following solution of hematoxylin:

Ripened 10 per cent alcoholic hematoxylin.....	10 cc.
2 per cent acetic acid.....	90 cc.

7. Wash in distilled water.

8. Carry sections through Müller's fluid but do not leave them in it for more than a few seconds.

9. Wash and decolorize by the Weigert-Pal method. The sections decolorize much more quickly than those stained by the usual method. To guard against complete bleaching, it is necessary that the sections be handled individually and be left but a few seconds in the potassium permanganate. Usually it is enough to dip the section in and out, without loosing it from the hook. It is also advisable to use weaker concentrations of all the solutions used.

10. Wash thoroughly in distilled water and let the sections stand for half an hour in tap water.

11. Wash again in distilled water and dehydrate.

12. Clear with xylene and mount in balsam.

This stain does not give satisfactory results with tissues embedded in paraffin, even if the paraffin is completely removed. Double embedding with paraffin and pyroxylin is also unsatisfactory. It can, however, be used with glycol stearate material and pyroxylin-glycol stearate material, if the stearate is fully removed by soaking overnight in chloroform or soap solution in a sealed jar in the oven. It can also be used with frozen sections, best after fixation on the slide with egg albumin.

SUMMARY

1. Methods are enumerated for staining a variety of tissue elements in successive sections from the same block, after various types of fixation and embedding.

2. A technic is described for the application of the original Weigert stain to sections already cut from material fixed in formaldehyde and embedded in pyroxylin. Its essential feature is the application of the "rapid mordant" to sections from which the pyroxylin has been removed. It is rapid and dependable, and the results excel those obtained by the iron mordant methods.

Abstracts from Current Literature

Anatomy and Embryology

THE MORPHOLOGY OF THE NEURONES MIGRATED FROM THE GANGLION NODOSUM OF THE VAGUS IN BIRDS. MARGARET E. BROWN, J. Comp. Neurol. **63**:127 (Dec.) 1935.

This is a study of neurons dislocated from the ganglion nodosum of newly hatched chicks, to determine whether such cells are normal or whether they show degenerative changes. The material examined was prepared by a modification of the reduced silver nitrate method of Cajal. The displaced neurons were observed in the sheath of connective tissue enclosing the ganglion nodosum and scattered along branches of the vagus nerve supplying the glomus caroticum and the ultimobranchial body. They occupy various positions either in the periphery of these nerves or among their bundles of fibers. A number were also observed embedded in the tissue of the ultimobranchial bodies.

The neurons of the sheath appear somewhat larger than the average cells of the ganglion. The cell bodies are not typically spherical but show irregular fibrous excrescences and lobulations. The nucleus is eccentric. The cells along the fiber bundles are more normal in size but are elongated. The cell bodies of the neurons scattered in the ultimobranchial body are more irregular than those of the normal neurons. Supernumerary processes issue from the cell body and its main prolongation. Except for the lack of capsule, these cells look like cells of the autonomic ganglion. Brown believes that these cells show evidence of changes of a regressive nature, that they left the ganglia as neuroblasts and that the growth of their main prolongations has been an attempt to establish normal connections.

FRASER, Philadelphia.

REACTION OF BLADDER TO STIMULATION OF POINTS IN THE FOREBRAIN AND MIDBRAIN. H. KABAT, H. W. MAGOUN and S. W. RANSON, J. Comp. Neurol. **63**:211 (Feb.) 1936.

The Horsley-Clarke stereotaxic instrument was used to explore every millimeter of the hypothalamus of the cat from a level close to the junction of the olfactory bulb and tract to as far caudally as a plane through the inferior colliculus dorsally and the middle of the pons ventrally. Each point stimulated was identified in stained sections. Thirty-eight cats were used, and 6,400 different points in the brain were stimulated. The contraction of the bladder always had the same characteristics, whether it was produced by stimulation of the telencephalon, the diencephalon or the mesencephalon. Near the anterior commissure in the ventromedial part of the telencephalon was a region where stimulation caused marked contraction of the bladder. The reactive zone does not correspond to any single cell group or fiber tract that has been described. In the diencephalon the areas which gave contractions of the bladder were the subfornical component of the medial bundle of the forebrain, the lateral hypothalamic area, the perifornical nucleus, the supra-optic commissure, the supramamillary commissure and the periventricular fibers. In the mesencephalon contraction of the bladder was produced by stimulation of the periventricular fibers, the central gray matter and the central tegmental fasciculus. Whenever any area which gave rise to contractions of the bladder was stimulated, the blood pressure changed and the pupils dilated. On stimulation of the telencephalic areas a marked decrease in amplitude and a moderate decrease in the rate of respiration were noted. In the diencephalon an increase in the rate and depth of respiration ensued. Vigorous and prompt contraction of the bladder was produced by stimulation of cells in the septum pellucidum and the preoptic area without a break as far caudally as the level of the

inferior colliculus. At every frontal plane explored only a small localized area yielded this response. By this method no evidence was obtained that the pathway for contraction of the bladder has its origin in the cerebral cortex. This paper deals with experiments on cats under pentobarbital sodium anesthesia. In a different series reported previously, the authors found that stimulation of the preoptic area, the septum pellucidum and the lateral hypothalamic area in waking animals evoked urination.

FRASER, Philadelphia.

GROWTH RESPONSES OF SPINAL NERVES TO GRAFTED BRAIN TISSUE. S. R. DETWILER, J. Exper. Zoöl. **74**:477 (Nov.) 1936.

Various portions of the brain of embryos of Amblystoma punctatum were grafted from three to four body segments caudal to the region of the anterior limb, after excision of the limb rudiment. Host embryos ranging from Harrison's stage 25 to stage 29 and donors from stage 21 to stage 31 were used, in order to test any effect of differences in the proliferative capacity of the grafts on the growth of the spinal nerves. When telencephalon median, diencephalon or mesencephalon were thus grafted, spinal nerves from higher levels did not grow caudally to the graft as they do when the limb, the optic cup or the nasal placode is grafted in the same position. Spinal nerves from the same segmental levels as those occupied by the transplanted brain made connection with fibrous outgrowths from the brain graft in 80 per cent of cases. There was no evidence that the age either of the donor or of the host material had any effect on the connection of the spinal nerves of the host with the grafted brain. The assumption that forces associated with proliferation of grafted structures are responsible for the altered course and convergence of spinal nerves toward that structure fits the facts in instances in which the limb, eye or nasal placode is grafted, but it appears less applicable to cases in which brain grafts are made. Induced limbs were observed only in instances in which the brain graft was accompanied by a nasal placode (telencephalon graft). This does not imply that the nasal placode can be regarded as a specific inductor, for many cases have been observed in which various other grafted structures have caused induction of a limb. In 29 per cent of cases the grafted brain was accompanied by masses of cartilage which presumably developed from the ganglionic crest cells taken with the brain graft, thus supporting the observations of others that the neural crest cells give rise to cartilage.

WYMAN, Boston.

A FIBER TRACT FROM THE LAMINA TERMINALIS IN BIRDS. LEONARDO DONATELLI, Neopsichiatria **1**:58, 1935.

A fiber tract from the lamina terminalis into the anterior wall of the infundibulum by way of the suprachiasmic stratum is demonstrated in birds. Donatelli considers it homologous with the prethalamohypothalamic tract in fishes (Kappers), the preoptic tract in amphibians (Roethig) and Staderini's bundle in mammals.

ALEXANDER, Boston.

POVERTY OF MEDULLARY SHEATH IN THE CENTRAL VEGETATIVE STRUCTURES OF THE BRAIN. HANS DIETRICH PACHE, Arch. f. Psychiat. **104**:137 (Sept.) 1935.

Pache carried out histologic studies of the "vegetative centers" of the brain (the medulla, midbrain and diencephalon and both the nuclei of the cranial nerves and the superimposed centers), with a comparison of nearby structures. He observed that macroscopically the vegetative centers, such as the nucleus of the vagus nerve, show a peculiar gelatinous, bluish, partly transparent picture, as compared with the whitish hue of the other nuclei. Histologically, when the sections are stained by the Weigert method, the vegetative centers show a striking lack of medullary sheaths, whereas the Bielschowsky method demonstrates a number of axis-cylinders, which is more or less equal to that in other nuclei. Staining by methods for glia fibers shows that the difference does not depend

on a variation in the number of fibers. When one takes into consideration that peripheral vegetative nerves are also characterized by poverty, or even absence, of medullary sheaths, one comes to the conclusion that this is a characteristic of the vegetative nervous system. Pache advances the theory that this observation is related to the fact that the vegetative nervous system is more primitive and less differentiated than the rest of the nervous system.

MALAMUD, Iowa City.

IS ALL THE COLLOID OBSERVED IN THE MIDBRAIN OF HYPOPHYSIAL ORIGIN? E. SCHARRER, Frankfurt. Ztschr. f. Path. **47**:134, 1935.

Clinical and physiologic observations reveal that symptoms similar to those produced by extirpation or destruction of the hypophysis can result also from pathologic changes of the nerve substance of the tuber cinereum. This and other observations prove the presence in the midbrain of several of the hormones of the hypophysis. According to Collin, the hypophysial colloid is transported to the midbrain along the nerve fibers and through the Virchow-Robin spaces and stored in the nucleus supra-opticus and nucleus paraventricularis. Scharrer, however, believes that not all the colloid is transported into the midbrain but that some of it is produced locally. He examined histologically a great number of brains of mammals, reptiles, amphibia and fish and observed intracellular and extracellular colloid in the region of the nuclei mentioned. As the colloid was regularly seen in the midbrain in numerous animals of various species, it cannot be regarded as a product of degeneration or as an artefact.

SAPHIR, Chicago. [Arch. PATH.]

THE NUCLEUS OF THE POSTERIOR LONGITUDINAL BUNDLE, THE FIBERS ARISING THEREFROM AND THE PROBABLE RELATION OF BOTH TO AUTOMATIC POSTURE OF THE HEAD. E. L. WENDEROWIČ, Monatschr. f. Psychiat. u. Neurol. **94**: 55 (Sept.) 1936.

That the posterior longitudinal bundle is the first structure to become myelinated in the brain indicates that it must be associated with a fundamental function of the vertebrate organism. Such a function cannot be attributed to conjugate movements of the eyes, which are controlled through this tract. It is likely, therefore, that the posterior longitudinal bundle contains fibers which serve an earlier and more important purpose. A clue to the problem has been provided by the observations of Fish, Windle and West, who showed that stimulation of the semicircular canals in the embryo of the cat first produces movements of the head, deviation of the eyes occurring only at a later stage of development. Fibers from the posterior longitudinal bundle have been traced to the nucleus interstitialis, which Wenderowič prefers to call the nucleus of the posterior longitudinal bundle. Ascending fibers can be seen ending in this nucleus in the 8 day embryo of the cat. The posterior longitudinal bundle also contains descending fibers, which arise from the nucleus interstitialis. It has been thought that they go only to the nuclei of the nerves supplying the ocular muscles. By means of the Marchi method, however, Wenderowič observed that, instead of going to these nuclei, they proceed in undiminished number through the brain stem to the lowest cervical segment of the spinal cord, where they end about the anterior horns. According to Wenderowič, these descending fibers carry the impulses which arise from stimulation of the semicircular canals and cause movements of the head and neck. The nucleus interstitialis receives impulses from ascending vestibular neurons of the second order and transmits them to the nerves which are concerned with the movements in question. In support of this view it is pointed out that the other parts of the aforementioned system show early myelinization. Thus, the vestibular nerve is the first cranial nerve to become myelinated, and the anterior roots of the cervical nerves receive their myelin sheaths earlier than other spinal roots. From observa-

tions on new-born rats, it appears that postural movements of the head in response to stimulation of the labyrinth represent an earlier and more fundamental activity than movements of the eyes. Cervical reflexes direct the whole motor system of the organism. It is therefore natural that their morphologic apparatus should develop before other systems. In spite of the fact that direct intracrural connections have not been demonstrated between the vestibular nuclei in the brain stem and the red nucleus, the red nucleus has been regarded by Magnus and de Kleyn as the center for labyrinthine reflexes controlling posture of the head in the cat. In the opinion of Wenderowič, the nucleus of the posterior longitudinal bundle represents the chief, and perhaps the exclusive, center for such postural control.

ROTHSCHILD, Foxborough, Mass.

Physiology and Biochemistry

PHYSIOLOGIC EFFECTS OF ACETYL-BETA-METHYLCHOLINE (MECHOLYL) AND ITS RELATIONSHIP TO OTHER DRUGS AFFECTING THE AUTONOMIC NERVOUS SYSTEM. ABRAHAM MYERSON, JULIUS LOMAN and WILLIAM DAMESHEK, Am. J. M. Sc. **193**:198 (Feb.) 1937.

This study was carried out on twenty patients, eighteen of whom had dementia praecox and two dementia-paralytica. Subcutaneous administration of 30 mg. of acetylbetamethylcholine (mecholyl) resulted in flushing of the face and chest, moderate or marked perspiration, salivation, rhinorrhea and lacrimation, a moderate fall in the blood pressure (from 4 to 54 mm. of mercury), a rise in the pulse rate (from 8 to 56 beats per minute) and a rise in the cerebrospinal fluid pressure (from 30 to 140 mm. of water). The effects of doses of 5 mg. were considerably less. Regardless of whether 1/100 grain (0.6 mg.) of atropine sulfate was given subcutaneously after or simultaneously with acetylbetamethylcholine, the vasomotor and secretory effects were readily prevented or checked. Pronounced antagonism of the two drugs was shown, the combined reaction depending on the quantities and the route of administration. Large preliminary doses of atropine sulfate prevented the usual marked fall in blood pressure produced by mecholyl.

The combined effect of intravenous injection of sodium amytal (from 0.5 to 0.7 Gm.) and 30 mg. of mecholyl on the blood pressure is additive, the resultant fall in blood pressure (from 28 to 82 mm. of mercury) being great in the four cases studied. When acetylbetamethylcholine (30 mg.) and epinephrine (0.5 cc.) were given subcutaneously the effects appeared to be those of mecholyl alone. When the epinephrine was given intravenously, however, the reaction of the blood pressure to this drug overshadowed that to mecholyl. The same principle applies to the combined effects of acetylbetamethylcholine and benzedrine. Contrary to the belief expressed by Starr, Elsom and Reisinger, the increase in pulse rate following administration of mecholyl is not a compensatory response to the change in blood pressure. Other observations of the authors show that preliminary administration of atropine completely inhibits the other effects of mecholyl.

MICHAELS, Boston.

URINARY PORPHYRINS IN DISEASE. KONRAD DOBRINER, J. Biol. Chem. **113**:1, 1936.

Normal human beings excrete coproporphyrin I in the urine. In patients suffering from catarrhal jaundice, hemolytic jaundice and Hodgkin's disease its excretion is increased. This result occurs either as heightening of a normal process or as failure of the tissues to complete a normal synthesis. In contrast, a few diseases of the liver—pigmentary cirrhosis (hemosiderosis) and tumor—lead to the excretion of coproporphyrin III. The latter substance may be derived from abnormal degradation of hemoglobin or from a part of the cellular elements of the respiratory system.

PAGE, New York.

THE EFFECT OF LIBERAL INTAKES OF CALCIUM OR CALCIUM AND PHOSPHORUS ON GROWTH AND BODY CALCIUM. E. W. TOEPFER and H. C. SHERMAN, J. Biol. Chem. **115**:685, 1936.

Increase in the calcium or calcium and phosphorus contents of an already adequate diet resulted in more rapid and efficient growth in rats, with greater economy in the use of the food. The rate of normal calcification, as shown in young of the second generation, was also increased. On diets known to be adequate in other respects, the full advantage to growth and apparent general health and vitality seemed to have been attained at a level of intake of 0.64 per cent of calcium in air-dried food mixture; further increase to 0.8 per cent of calcium may still further increase the rate of calcification.

Thirty day old rats from families kept on an adequate diet of nearly minimal calcium content (0.2 per cent) had about 0.6 per cent of the body calcium of normal adults; those from families in which the food contained 0.64 per cent calcium (a ratio of calcium to phosphorus of 1.5) had about 0.8 per cent of the normal calcium, and those from families the food of which contained 0.8 per cent calcium (a ratio of calcium to phosphorus of 1.5) had about 0.9 per cent of the normal adult amount.

In the experiments reported here, increase in the calcium content of an adequate diet to 0.8 per cent of the weight of the dry food mixture has not revealed any unfavorable result to throw doubt on the advantage of the increased rate of growth and normal calcification.

PAGE, New York.

THE CARBOHYDRATE METABOLISM OF BRAIN: III. ON THE ORIGIN OF LACTIC ACID. STANLEY E. KERR and MUSA GHANTUS, J. Biol. Chem. **117**:217, 1937.

Kerr and Ghantus had shown previously that the free sugar content of the brain varies normally from 35 to 75 mg. per hundred grams in rabbits and from 45 to 86 mg. in dogs. Lowering of the blood sugar by poisoning with phlorhizin or by insulin causes a corresponding decrease in the amount of free sugar in the brain. Hyperglycemia caused by pancreatectomy or by administration of dextrose causes a rise in the amount of sugar in the brain. The free sugar content of the brain was constantly lower than that of blood, except in extreme insulin hypoglycemia. Neither the lactic acid nor the phosphocreatine of the brain was affected significantly by any of the experimental conditions.

During postmortem autolysis the free fermentable sugar of the dog's brain disappears within from three to five minutes, and from 80 to 85 per cent of the glycogen is lost within fifteen minutes. The amount of lactic acid found during a two hour period of anaerobic incubation corresponds to the loss of glycogen and free sugar. It appears that during the first three minutes of autolysis the production of lactic acid corresponds to the combined fall of free sugar and glycogen, whereas after that time it is accounted for by the decrease in glycogen alone. When the sugar content of the blood is either raised or lowered, the amount of lactic acid in autolyzed brain again parallels the amount of free sugar and glycogen available. From these data Kerr and Ghantus appear to have shown conclusively that both the glycogen and the free sugar of the brain are precursors of lactic acid.

PAGE, New York.

VASOMOTOR RESPONSES IN HEMIPLEGIC PATIENTS. G. STÜRUP, B. BOLTON, D. J. WILLIAMS and E. A. CARMICHAEL, Brain **58**:456, 1935.

In this study the authors observed the effects produced by vasoconstriction and vasodilatation in normal persons and in patients suffering from cerebral lesions. Dilatation and constriction were produced by immersion of the indifferent limbs in tanks of warm and then of cold water. Simultaneous temperature readings were obtained from the cheeks and the tips of the digits of the hands and feet by means of thermocouples. Rectal temperatures were registered by a thermocouple inserted 5 or 6 cm. above the anal sphincter.

In normal subjects the rises in temperature of the digits of similar limbs are synchronous, when the method of immersion is used. The face warms first, then the hand and last the foot. The rise in temperature of the digits occurs only after the rectal temperature has risen, but it is not dependent on the actual rectal temperature. After cooling, like digits of two limbs show a similar and synchronous fall of temperature.

Similar studies were made on patients with varied types of cerebral lesions. The authors conclude that vasodilatation and vasoconstriction of the limbs in response to warming and cooling of the body are not affected in degree or in time of onset by lesions of the cerebral hemispheres. However, in three cases in which marked spasticity existed, cooling of the hemiplegic upper extremity was slower and more irregular than that of the normal limb. Observation showed that in each of these cases the affected limb was spastic and that during the time of cooling there was adduction of the arm with flexion of the fingers and wrist. The irregularity in the fall of temperature of the digits on the affected side took place when the limb was moved. In such cases the digits of the lower limb showed a fall in temperature which was equal and regular on the two sides. No alteration in posture of the lower limbs took place during the cooling. As a result of movement of the upper spastic limb during cooling, the fingers are brought close together and nearer the body. Closing the fingers causes approximation of comparatively warm surfaces and prevents free cooling of these surfaces. In this way, loss of heat may appear more slowly in the digits of the hemiplegic limb than in those of the opposite, healthy limb. That the hemiplegic posture adopted in these patients is of importance is evidenced by an experiment using normal subjects. In normal subjects cooling was equally rapid on the two sides after immersion, but when one limb adopted the hemiplegic posture cooling was less rapid on that side.

It was observed in one or two patients that immersion of the feet in cold water was followed by immediate, but short-lived, cooling of the hands, with subsequent warming and then marked cooling. The second cooling synchronized with the fall in rectal temperature. Thus, it may be deduced that on immersing the limbs in cold water, two mechanisms play a part in bringing about cooling of the upper limbs: first, a sensory stimulus producing vasoconstriction and, second, vasoconstriction dependent on the fall of temperature of the blood.

The work described by the authors favors the view that lesions of the cerebral hemispheres do not alter in any way the functional capacity of the blood vessels of the hemiplegic limb to constrict in response to a sensory stimulus or to a fall in blood temperature and, second, that, provided an adequate warming stimulus is presented, the blood vessels of the hemiplegic limb will dilate as in the normal limb.

SALL, Philadelphia.

DEPRESSANT PERIPHERAL EFFECT OF PROSTIGMIN AND ITS TEMPORARY ANTAGONISM BY CURARINE. GRACE BRISCOE, J. Physiol. **86**:1P, 1936.

In the course of a study of the antagonism of prostigmin (the dimethylcarbamic ester of 3-oxphenyltrimethylammonium methylsulfate) to curarine, experiments made as controls on the action of prostigmin alone revealed a characteristic depressant effect when the circulated nerve-muscle preparation was tested with different rates and strengths of stimulation. With dial anesthesia or in decerebrate preparations without dial, a fast rate of stimulation (from 150 to 160 per second) produces a larger contraction than a slow rate (from 25 to 35 per second). Curarine in moderate doses has a depressant effect on responses to all rates and affects postural contractions (due to slow rates) markedly and rapidly. Responses to fast rates remain always larger than those to slow rates. Prostigmin (in unpoisoned muscle) has a different effect. In a few minutes after intramuscular injection the response to fast rates becomes progressively smaller and more quickly depressed. In from ten to thirty minutes the response to a fast rate is twitchlike and considerably smaller than the response to a slow rate. The response to the slow rate can maintain a postural contraction, although its initial curve of contraction is altered. If curarine is now given intravenously,

0.3 mg. per kilogram of body weight, a dose normally sufficient to produce twitchlike responses to all rates, the onset of this characteristic effect is delayed for a few minutes, and meanwhile antagonism to the depression from prostigmin is seen. Within a minute the response to fast rates is altered in that it becomes larger and less twitchlike; in two or three minutes it is larger than the response to slow rates, as the latter is now depressed by the action of curarine. In from five to ten minutes the typical effects of curarine is seen, fast rates producing larger twitches than slow rates. Recovery from this condition takes place more quickly than in the absence of prostigmin. After recovery, another dose of curarine will quickly produce twitchlike responses, without reversal of size.

ALPERS, Philadelphia.

THE EFFECT OF THE CAROTID SINUS ON THE VENOUS FLOW. R. J. S. MCDOWALL, J. Physiol. **86**:7P, 1936.

In an animal in good condition, the first effect of reduction in the pressure of the carotid sinus is an increased flow from the femoral vein. This is followed by slowing, if the peripheral vascular constriction is sufficiently severe, as may occur if the aortic depressor nerves have been previously cut. These results are in accordance with the increased venous pressure and cardiac output already described for mild degrees of loss of normal depressor activity. They emphasize that an important function of the depressor mechanism is the control of circulatory capacity.

ALPERS, Philadelphia.

THE BERGER RHYTHM IN THE MONKEY'S BRAIN. E. D. ADRIAN, J. Physiol. **87**:83P, 1936.

In rhesus monkeys under dial anesthesia groups of Berger waves occur mainly in the striate area; the rest of the cortex tends to give irregular rhythms, though occasional groups of 10 per second can be recorded. The groups in the striate area seem to arise and subside spontaneously, at intervals of from two to ten seconds (depending on the depth of anesthesia); apart from these there is little activity as long as the animal is in the dark. With suitable anesthesia, illuminating the eyes has a twofold result. The immediate effect is an outburst of rapid, irregular oscillations, lasting for one-half second or more; this is followed by a group of waves at 10 per second, resembling those which occur spontaneously. When the light is turned off, there is a renewed irregular discharge of short duration, and this again is followed by a train of waves of the spontaneous type, at 10 per second. Thus, illuminating or darkening the eyes throws the striate area into activity giving the rapid, confused electrical effect which would be expected, and this activity arouses the cortex to produce a group of spontaneous waves. Presumably, it does so by causing some degree of "facilitation," which raises the excitability of the neurons to the level required for a spontaneous discharge.

This result throws light on the change from sleep to waking in man. During deep sleep, with the eyes closed and the muscles relaxed, there will be little induced activity in the cortex, and, in the absence of facilitation, the excitability of the neurons will fall to a very low level. In very deep sleep the Berger waves occur infrequently, or not at all (Adrian and Yamagiwa, 1935; Loomis and others, 1935). Adequate sensory stimulation causes return of the waves, without necessarily arousing the sleeper. The activity induced in the cortex must have produced some general facilitation, but this tends to subside if the stimulation is not repeated. If it is repeated until the sleeper wakes, the waves may become almost continuous as long as the eyes are closed though they cease as soon as the eyes are opened. The cortical excitability will now have been raised to the waking level, for the stimulation will have produced movement and a return of tone in the muscles; thus, sensations from the limbs will reenforce the initial facilitation. When the eyes are opened, the spontaneous waves will be superseded, as in the monkey, by more rapid and asynchronous activity.

Various differences are to be expected between the state of the cortex in man when asleep and that in the monkey under dial anesthesia. The most obvious difference is that the monkey cannot be awakened. Clearly, dial is not equivalent to the factor (hypothalamic?) which is responsible for the regular cycle of sleep and waking. It is probable, however, that the rapid changes from sleep to waking and vice versa induced by opening and closing the eyes and by other sensory stimulation operate mainly by changing the level of facilitation in the cortex This hypothesis differs little, if at all, from that advanced by Kleitman (1929).

ALPERS, Philadelphia.

INHIBITION AND EXTINCTION OF SENSITIVE POINTS OF THE SKIN. S. W. GOLMANN, Encéphale **31**:176, 1936.

Clinical evidence is presented for the "extreme lability of the excitable elements" of the skin, as opposed to the classic concept of a "mosaic" of constant points, each having a specific sensory receptivity to heat and cold. Thus, in a case of meralgia paraesthetica light contacts over the lateral aspect of the thigh produced painful sensations in the territory of the lateral femoral cutaneous nerve. The painful sensation did not appear when the skin of the anterior surface of the thigh was lightly pinched or pressed. The same stimuli, as well as heat or cold, when applied to the opposite extremity or to different nerve territories, had no inhibiting effect on the painful sensation, thus showing that the inhibition was not due to distraction of attention. Similar relations were observed in several other cases of meralgia, in a traumatic lesion of the sciatic nerve and in tabes. Three tabetic patients presented the plantar phenomenon of Rubens Hirschberg, consisting of intense, burning pain on slight superficial stimulation of the sole of the foot. The pain could be attenuated or completely suppressed by compressing the sole of the foot immediately after the pain-producing stimulus, by touching the sole with a tube containing water at 40 C. or by tickling the sole. In a case in which the pain persisted long after cessation of the stimulus, it could be extinguished by tickling but reappeared as soon as this ceased. By repeated tickling the pain could thus be made to disappear and reappear successively five or six times. In certain tabetic patients a pinprick is first felt as dull and only from five to eight seconds later as sharp. In a patient with tabes light rubbing of the stimulated point immediately after the "dull" response prevented the "sharp" sensation from appearing. Patients suffering from painful nerve disease often discover a stimulus which attenuates the pain. In every-day life pain resulting from intense heat is attenuated by friction of the affected area, pruritus by scratching, etc. These observations are in keeping with those of Waterston, who found that the specific sensory points of the skin fluctuated from one examination to the next. Leriche likewise found no constant hot or cold points and regarded all modes of common sensation as modifications of touch. Golmann concludes that the "mosaic" of sensory points of the skin changes unceasingly under the influence of stimulation of neighboring areas, of previous stimulation and of processes taking place in sensory centers, such as the thalamus and cortex.

LIBER, New York.

SYMPTOMATOLOGY OF NARCOLEPSY AND ITS TREATMENT. M. NAGY, Monatschr. f. Psychiat. u. Neurol. **89**:286 (Sept.) 1934.

Nagy discusses the symptomatology of narcolepsy and the various theories advanced to explain its origin. He reports six cases. Four patients were treated by the method of suboccipital injection of air introduced by Benedek and Thurzó. Cerebrospinal fluid is withdrawn by cisternal puncture, and from 10 to 20 cc. of air is injected. The injections are repeated, if necessary. In one case seven treatments were given. Two patients ceased to have narcoleptic attacks, and two showed marked improvement. The favorable effect of introducing air into the ventricular system is attributed to slight hyperemia of the vegetative centers concerned in regulating sleep, with consequent improvement of the blood flow and exchange of fluid in these areas.

ROTHSCHILD, Foxborough, Mass.

THE ACTION OF YOHIMBINE ON THE AUTONOMIC NERVOUS SYSTEM. PETER WEGER, Upsala läkaref. förh. **41**:191 (Dec.) 1935.

This is an experimental investigtaion dealing with the action of yohimbine on the autonomic vegetative nervous system. The experimental animals used were cats, guinea-pigs, rabbits, frogs and fish. Weger found that yohimbine produces a transitory motor effect on the isolated frog's heart. He obtained a similar response with the cat's heart in situ. This action, however, changed after a time into a progressive inhibitory effect and, finally, into a reversed action. The inverse bradycardia was eliminated with the aid of atropine. In a Trendelenburg preparation perfused according to Backman, yohimbine in weak solutions produced fleeting dilatation of the blood vessels followed by vasoconstriction, while stronger concentrations caused immediate constriction of the vessels. The vasoconstricting effect of epinephrine was weakened after the administration of yohimbine, and when strong concentrations were used, dilatation of the vessels occurred. This altered response of the blood vessels to epinephrine persisted for a time after flushing the circulatory system with Göthlin's solution. Barium chloride invariably produced vasoconstriction after the administration of yohimbine in any concentration.

When injected subcutaneously, yohimbine produced a drop in body temperature in rats, guinea-pigs and rabbits. This fall of temperature could be prevented by keeping the animal in a chamber at 26.5 C. Shaved rabbits reacted to yohimbine with a greater fall of temperature than unshaved rabbits. This hypothermia can be intensified by preliminary administrations of small doses of epinephrine, which by themselves are without effect. When applied in small or moderate concentrations, yohimbine caused no change in oxygen consumption of the muscle tissue of rats. In strong concentrations it produced a decrease in oxygen consumption. When injected subcutaneously into rats, yohimbine produced no particular change in the basal metabolic rate of the animals during the next four hours. It reduced a basal metabolic rate previously increased with the aid of epinephrine. In high concentrations yohimbine caused a notable motor action in the isolated rabbit's heart. This action could not be abolished with the aid of atropine. In increasing concentrations yohimbine weakened, removed and even altered the motor action of epinephrine and barium chloride on the isolated rabbit uterus. Strong concentrations of yohimbine weakened the effect of pilocarpine on the uterus. The normal reaction of the uterus could be restored with repeated washings in Tyrode's solution. The response to pilocarpine and barium chloride returned quicker than that to epinephrine.

In moderate doses yohimbine caused a mild motor reaction of the isolated small intestine of the rabbit. When stronger concentrations were used, the effect was inhibitory. The inhibitory reaction of epinephrine was easily weakened and even abolished with the aid of moderate concentrations of yohimbine. The same concentrations had little influence on the motor activity of parasympathetic drugs, especially barium chloride. The response to the parasympathetic drugs and to barium chloride returned rapidly after repeated washings with physiologic solution of sodium chloride; the response to epinephrine is delayed.

Yohimbine interfered with the secretory action of epinephrine on the cutaneous mucous glands of the frog. It removed the blanching of the frog's skin produced through subcutaneous administration of epinephrine. Yohimbine weakened the clustering effect of epinephrine on the chromophores in the isolated skin of Phoxinus laevis. It may abolish the clustering of pigment cells and even reverse the process, causing dispersion. Weger believes that yohimbine, like ergotoxine, possesses two different peripheral pharmacodynamic actions: one, a stimulating effect on the organ cells which are supplied by the autonomic vegetative nervous system, the other a paralyzing action on the sympathetic nerve endings.

NOTKIN, Poughkeepsie, N. Y.

Neuropathology

CASE OF THREE NEOPLASMS. B. C. PORTUONDO, Am. J. Cancer **28**:752 (Dec.) 1936.

Portuondo cites a case of three dissimilar types of tumor. Two of these and a metastasis from the third were within the cranial cavity. The hypernephroma in all probability represented a cell rest which had become neoplastic. The acoustic neurofibroma may also have had its origin in a cell rest which became active. The peripheral areas of the neurofibroma contained many whorls of spindle-shaped cells, while in the more central portions only a few such cells lay in a stroma composed of cells having small, round nuclei and fusion of membranes to form a tenuous background. The carcinoma of the pituitary gland would seem to have no demonstrable relationship with any cell rest. From the history it appeared that the acoustic neurofibroma was of about four years' standing. Visual disturbances were marked a year and a half prior to death, which indicates that the pituitary tumor was large enough at that time to cause ocular signs and symptoms. The weakness, listlessness and hypotension may have been due to the hypernephroma, and, since these symptoms were of about five years' duration, it would seem that the tumor of the kidney had been present about that length of time. The cerebellar metastasis may have been responsible for the slow, slurring speech and the staggering gait. These occurred only about two months prior to death, which would indicate that the metasasis may have occurred at that time, although it may have been present longer without causing enough destruction of cerebellar tissue to produce signs. The added presence of the hypophysial carcinoma suggests a special tendency to neoplasm, and it may be that this was the decisive factor.

EDITOR'S ABSTRACT. [J. A. M. A.]

DIFFUSE CEREBRAL CHANGES IN POISONING WITH OIL OF CHENOPODIUM. SAMUEL D. INGHAM and CYRIL B. COURVILLE, Bull. Los Angeles Neurol. Soc. **1**:152 (Dec.) 1936.

Ingham and Courville, in a brief discussion of the literature on chenopodium poisoning, point out that the toxic symptoms which may follow the use of this anthelmintic drug include, beside gastro-intestinal disturbances, tinnitus and deafness most frequently, but occasionally pathologic reflexes, hemiplegia, muscular rigidity, aphasia, delirium, coma and convulsions. Autopsies performed in such cases have not included a careful examination of the nervous system; Ingham and Courville report a case in which a neuropathologic study was made.

A married woman aged 25 took 10 minims (0.616 cc.) of oil of chenopodium three times a day for six days, a total of 180 minims (11.09 cc.). Restlessness and sleeplessness were followed by incoherence, disorientation and delirium. A day or two after the last dose convulsions began; they recurred several times a day. Examination revealed: rectal temperature, 102 F.; pulse rate, 122 and blood pressure, 122 systolic and 82 diastolic. The patient was in a state of restless coma, struggling at restraints. There was no paralysis, but the tendon reflexes were increased in the lower extremities, with ankle clonus and a positive Babinski sign bilaterally. The convulsions were generalized and associated with carpal spasm and were followed eventually by extensor rigidity. The spinal fluid was normal. The temperature rose gradually to 105 F. Edema of the face and lungs developed, in the presence of continued convulsions and coughing of frothy mucus. Death occurred on the fourteenth day after the first dose of oil of chenopodium.

Examination of the brain revealed cerebral congestion and edema, with a few hemorrhages. There was cellular proliferation of the arachnoid and the cortical blood vessels, while the nerve cells in the cortex, particularly the small pyramidal cells, showed acute swelling. There was also acute swelling with loss of tigroid granules in the Purkinje cells of the cerebellum. Some of the ganglion cells contained excess lipoid pigment. The cellular changes were most advanced in areas in which vascular proliferation was most active. These changes, the authors think, were due to the direct toxic effect of the drug on the nerve tissue.

MACKAY, Chicago.

MULTIPLE METASTATIC TUMORS IN THE BRAIN ARISING FROM PRIMARY BRONCHIAL CARCINOMA. W. E. CARNEGIE DICKSON and C. WORSTER-DROUGHT, J. Neurol. & Psychopath. **16**:289 (April) 1936.

The increasing incidence of bronchogenic carcinoma, with a tendency to produce metastases in the brain, has been reported of late. The latency of the pulmonary symptoms and the almost complete dominance of the clinical picture by cerebral symptoms have led to difficulties in diagnosis. The primary focus in the lungs is frequently missed on account of its small size. The cerebral metastases often grow into, or are in continuity with, the choroid plexuses of the lateral ventricles. Their histologic structure is papillomatous. Because of this, they have often been designated erroneously as primary malignant tumor of the choroid plexus. On the basis of a study of fourteen cases, the authors are convinced that these tumors are metastases secondary to primary bronchogenic carcinoma. They are in agreement with Bailey that a primary thoracic tumor must be considered in cases of rapidly developing intracranial symptoms when occurring in patients of middle age. The cerebral tumor is frequently cystic. As an aid to diagnosis, fluid aspirated from the cyst will be observed to contain sputum-like material, with fragments of columnar epithelial cells resembling those seen in catarrhal bronchitis. Mucin may also be demonstrated. Primary bronchial carcinoma may be: (1) a sclerosing bronchial growth, (2) a small nodule in connection with a secondary or tertiary bronchus and (3) a large tumor at the periphery of the lung. Careful sectioning of the lung is often necessary to demonstrate the tumor. The most common cerebral symptoms are: headache, mental confusion, memory defects, change in temperament, signs of papilledema and changes in the deep and plantar reflexes. Cerebral metastases are multiple and are most common in the frontal and temporosphenoid lobes, as well as in the cerebellum; because of their malignant nature, the outcome is usually fatal.

N. MALAMUD, Ann Arbor, Mich.

OLIVOCEREBELLAR ATROPHY. D. NOICA, J. NICOLESCO and T. HORNET, Encéphale **31**:372, 1936.

The authors report the case of a man aged 28 who had suffered from nervous disturbances for a little over four years. The illness began with sudden faintness and a fall off a roof, 8 meters high. The patient was unconscious for eight days, after which he showed weakness and generalized muscular hypotonia, station and gait with a wide base, oscillations of the trunk, small steps, nystagmoid movements of the eyeballs, slowness of all voluntary movements, retropulsion and bilateral lateropulsion, bilateral combined flexion of the pelvic extremities, pendulous knee jerks and abolition of the postural reflexes. Speech was of the cerebellar type, but this was stated to have been the condition since childhood. The patient was left handed. There was no disturbance of sphincteric, intellectual or sensory functions, except diffuse pains. Vestibular caloric and rotatory tests gave normal results. The spinal fluid showed nothing abnormal. The patient died of chronic pulmonary tuberculosis. Necrospy showed atrophy of the entire cerebellum, which was of about two-thirds the normal dimensions. Atrophy of the vermis was most marked. Microscopically, the atrophy involved the cortex, white matter and central nuclei and the bulbar olives and parolives bilaterally. The lesions were exclusively degenerative and consisted mainly in diminution in the number of ganglion cells and nerve fibers, including the axons and myelin sheaths. The olivary lesions were most intense in the dorsomedial portions of the principal olive and in the dorsal parolive. The superior cerebellar peduncles were well stained in myelin preparations but were relatively atrophic. The medullary feltwork about the red nucleus, the middle cerebellar peduncle, the temporopontile fibers, the bundle of Helweg on both sides and the white matter of the medulla about the convexity of the olives were somewhat pale. The inferior cerebellar peduncles were atrophic. In the lumbar region of the spinal cord was a small cavity in the neighborhood of the central canal. A small bundle of direct spinocerebellar fibers was absent

bilaterally. The cells of Clarke's column were normal. The lesions were predominantly paleocerebellar, although all parts of the cerebellum and associated organs were involved. The absence of intention tremor is attributed to the relative preservation of the dentatorubrothalamic path and to the probable compensatory activity of other structures in the brain stem.

LIBER, New York.

SELECTIVE INVOLVEMENT OF THE LAYERS OF THE CEREBRAL CORTEX IN MENTAL DISEASE. MAXIMILIAN ROSE, J. f. Psychol. u. Neurol. **47**:1 (May) 1936.

Rose examined the regio entorhinalis and regio praesubicularis in cases of amaurotic idiocy, Pick's atrophy, Huntington's chorea and dementia paralytica. These two regions have a similar ontogenetic development and constitute histogenetically a related unit. In spite of this ontogenetic similarity, however, they reveal such architectonic variations that there can be little doubt that they subserve different functions. In view of this, Rose undertook to determine how histogenetically similar but architectonically different cortices in two regions subdivided into twenty-five areas react in four diseases of different etiology. If vascular or cerebrospinal fluid factors were the sole determinants of the pathologic process, one would expect that in all these diseases the same layers would be affected by the process. Rose did not find this to be the case in the brains which he examined.

In amaurotic idiocy the disease affected chiefly the lamina principalis interna, which had disappeared, whereas the lamina principalis externa showed much less and the lamina dissecans no architectonic alteration. In Pick's atrophy, however, the lamina principalis externa—especially its outer portion—was most severely affected, so that the lamina principalis externa alpha had completely disappeared, whereas the lamina principalis interna was somewhat less and the lamina dissecans was least affected. In Huntington's chorea, on the other hand, the architectonic changes were much less marked; they also affected chiefly the lamina principalis externa but, in contrast to the condition in Pick's disease, the brunt of the pathologic process was in its middle portion, whereas the lamina principalis interna showed slight changes and the lamina dissecans hardly any. In the case of dementia paralytica, in which the disturbance was severe, pathoarchitectonic changes, although observed in all layers, were more marked in the lamina principalis externa and the lamina principalis interna, whereas the lamina dissecans was relatively well preserved.

According to Rose, the various degrees of involvement of the different laminae in such dissimilar diseases must be attributed to variations in the physicochemical structure of these layers, for each layer apparently has an individual affinity for various noxae.

Examination of the affected areas also disclosed which components of a given layer were affected primarily and which secondarily. It could also be determined that in the respective diseases there was a definite chronological order of involvement, as far as the intensity of the process was concerned, which was characteristic for the disease in question; this was true not only of the principal regions but of the subregions. Thus, in amaurotic idiocy there were first affected the lamina principalis externa alpha and gamma and later delta and epsilon; in Pick's atrophy the lamina principalis externa alpha was first affected, later gamma and, finally, delta and epsilon; in Huntington's chorea, on the other hand, there were first affected the lamina principalis externa beta and gamma, later alpha and, finally, delta and epsilon. Of the principal layers of the lamina dissecans the cellular layer was least affected in all cases. This lamina apparently is most resistant to all pathologic processes.

In this connection, Rose points out the significance of the researches of Marinesco and Pighini on oxidases as an index of certain metabolic processes in the brain. Winkler was the first to demonstrate blue-stained granules in the protoplasm of lymphocytes stained with weak solutions of alphanaphthol and dimethylparaphenylenediamine. The blue staining of the granules is the result of indophenyl blue synthesis and occurs only in elements containing oxidases.

Utilizing this method, Marinesco demonstrated that the oxidase content varies in the different layers of the motor cortex; this was especially noticeable in the second and third layers, both of which were loaded with blue granules. Rose, in collaboration with Bielschowsky, confirmed Marinesco's observations in the motor cortex in five dogs and one ape. The lamina zonalis (I) contained only a few granules and the lamina corpuscularis (II) somewhat more, whereas the third layer was unusually rich in granules not only in the motor but in the other portions of the cerebral cortex. The deeper layers all appeared pale. Under higher magnification, however, the protoplasm of these cells did not appear to have more blue-stained granules than that of the cells in layer III; from this, one could assume that the granules were present not only in the ganglion cells but in the glial plasmatic ground substance. The greater content of tissue oxidases in the third layer of the cortex would seem to indicate that this layer has a special affinity for oxygen and is therefore much less resistant to most diseases than the other layers.

Rose and Bielschowsky also employed the indophenol blue reaction as an index for determining the differences in oxidase content of the various architectonic centers in the cornu ammonis. They observed that the cells in fields h 3, h 4 and h 5 contained fewer blue granules than those in fields h 1 and h 2. They also observed that in field h 2 the granules were present only in the ganglion cells, whereas in field h 1 they were observed also in the intercellular structure. The greater affinity for oxygen of field h 1 corresponds to the greater vulnerability of this area in various diseases. It seems, therefore, that in all patho-architectonic changes of the cerebral cortex there can be established an association between the pathologic process and the histogenetic, architectonic or histologic units. These units constitute, individually or in groups, functionally associated complexes, which Vogt designated as topistic units.

KESCHNER, New York.

PATHOLOGICOANATOMIC CHANGES IN EPILEPSY. M. MINKOWSKI, Schweiz. Arch f. Neurol. u. Psychiat. **37**:273, 1936.

In this review of the pathologicoanatomic picture in epilepsy, Minkowski presents the results of his own studies, particularly with reference to changes in the hippocampus, choroid plexus and inferior olive. The brains were taken from patients who died in status epilepticus. The changes were similar to those reported by Spielmeyer, but Minkowski is not convinced that they are entirely attributable to preparoxysmal vasospasm and ischemia, which are assumed to be characteristic of the initial phase of the seizure. At least part of the changes may be due to exacerbation of the underlying disease process, since the presence of similar alterations following death in the course of a single seizure would indicate their beginning prior to the convulsion. Vascular changes over the convexity during an attack do not prove the existence of similar phenomena in the deeper parts, nor has cerebral ischemia been universally accepted as the unvarying accompaniment of the epileptic seizure. Since some of the changes in the cornu ammonis are obviously chronic, they may be due to susceptibility of that region to certain noxae rather than to a local peculiarity in blood supply. The subject is best studied, therefore, by comparison of the chronic with the acute changes.

Thickening of the walls of the vessels involving particularly the smaller vessels and precapillaries has been observed in the brains of even young epileptic patients. Of the chronic parenchymatous changes in the cerebral cortex, sclerosis of the cornu ammonis stands in the foreground. The lesion is unilateral for the most part, and the incidence varies from 30 to 50 per cent, according to different authors. There is predilection for Sommer's sector and the end-plate, but other parts, including the so-called resistant dorsal cell band and the presubiculum, may be involved, although the fascia dentata is almost always spared. Sclerotic and degenerative changes in the inferior olive, usually bilateral, were observed by Minkowski in about three fourths of the cases of genuine epilepsy which he studied.

Similar alterations were observed in a case of eclampsia and in one of cerebral arteriosclerosis in which seizures were of only five months' duration, both patients having died in status epilepticus. The changes were lacking, however, in four cases of traumatic epilepsy. The phylogenetically younger lateral, dorsal and oral parts of the olive were generally more affected than the remaining portions. Glial changes show predilection for the subpial region (surface gliosis) and the lamina molecularis of the cerebral cortex. Although dysplastic anomalies which are often encountered in the choroid plexus in persons with epilepsy are not infrequent in the brains of normal adults, adhesions between the choroid tufts and the ventricular walls are usually frequent in the brains of epileptic patients.

In warning against the placing of too much emphasis on repeated vascular disturbances as the cause of the chronic changes, Minkowski points out that similar alterations are observed in association with other chronic diseases of the brain. However important the acute effects of the convulsive seizure, there may be produced through the mediation of the vascular disturbance and other factors a chronic epileptic noxa, which is active even in the interval between convulsions. Changes in the choroid plexus, glia, blood vessels and meninges suggest the existence of humoral, secretory and hydrostatic components in the etiology of epilepsy. So far as the pathologic changes are concerned, they are to be regarded as the facultative and variable anatomic correlates of a generalized disturbance, which is essentially dynamic.

DANIELS, Denver.

HEMORRHAGES INTO THE FLOOR OF THE FOURTH VENTRICLE IN INTOXICATIONS AND INFLAMMATIONS OF THE BRAIN. O. BERNER, Virchows Arch. f. path. Anat. **296**:636, 1936.

Berner had previously described the occurrence of multiple minute hemorrhages in the floor of the fourth ventricle following trauma to the head. Such hemorrhages were observed when the trauma and other evidences of injury to the brain were slight. They were usually situated just anterior to the striae acusticae and beside the median sulcus. They led Berner to state that the finer vessels of this region are especially susceptible to trauma. Duret had claimed that such hemorrhages are due to rupture of small vessels caused by the mechanical shock of the injury. Berner claims that they are the result of diapedesis. If the latter theory is true, similar lesions should be seen in nontraumatic conditions. He describes briefly the observations so far as hemorrhages into the floor of the fourth ventricle are concerned in five cases of acute methyl alcohol intoxication, one case of acute carbon monoxide poisoning and one case of acute poliomyelitis. The presence of hemorrhages in these conditions, as well as after trauma, leads Berner to maintain his position that the vessels of the floor of the fourth ventricle are more disposed to diapedesis than those of the rest of the brain.

SCHULTZ, Evanston, Ill. [ARCH. PATH.]

DIFFUSE LEMMOBLASTOSIS OF THE CENTRAL NERVOUS SYSTEM. K. VON SANTHA, Ztschr. f. d. ges. Neurol. u. Psychiat. **154**:763 (Feb) 1936.

In 1934 Foerster and Gagel reported diffuse infiltration of the brain and spinal cord with Schwann cells in a case of Recklinghausen's disease. Santha reports another case in which there was no neurofibromatosis. A girl aged 9 years, who was admitted to the University Hospital in Budapest on Oct. 11, 1934, had been well until Dec. 12, 1933. On that day she fell and struck her head. She was unconscious for half an hour and vomited for three days. For about a week she complained of headache and dizziness. A gradual change in personality and character appeared after the trauma to the head. She became dull and lost interest. She began to lose weight, and precocious hirsutism appeared. A roentgenogram of the skull in April 1934 showed a parieto-occipital fracture line. Frequently recurring epileptic seizures appeared in July 1934. Neurologic examination on July 30, 1934, gave negative results except for aphonia. Eight days

after lumbar puncture left hemiplegia suddenly developed. The Wassermann reaction and the gold curve of the spinal fluid were negative. On Aug. 20, 1934, left hemiplegia without sensory changes was found.

On admission to the hospital physical examination revealed obesity, with hypertrichosis and a blood pressure of 100 systolic and 74 diastolic. Neuropsychiatric examination revealed: hypomimia; defective blinking; slight spontaneous conjugate deviation of the eyes to the left and weakness of conjugate voluntary lateral gaze to the right; some dysphagia; left hemiplegia, including the face and the tongue on that side, with hyperreflexia and a positive Babinski sign on the left; absence of the abdominal reflexes on the left; diminution of the corneal reflexes, especially on the left, and palatoplegia, with particles of food resting on the larynx. The patient was apathetic, somnolent and emotionally unstable. She did not speak. There were delayed responses to simple commands during the examination.

A roentgenogram of the skull showed increased digital markings, widened sutures and a moderately widened sella. The temporal parts of the optic disks were atrophic; the nasal portions were edematous. Albumin and hyaline casts were present in the urine. Concentration tests of the urine gave normal results. The curve for sugar tolerance showed delay. The basal metabolic rate was minus 9.1 per cent; a urine test for pregnancy gave negative results; examination of the spinal fluid revealed: 7 cells, a total protein content of 30 mg. per hundred cubic centimeters and a sugar content of 85 mg. Epileptic attacks became increasingly frequent, and the patient died on October 29, of aspiration pneumonia.

The brain weighed 1,725 Gm.; it seemed larger and the ventricles smaller than normal. There was no change in the consistency of the brain. The corpora mamillaria, the tuber cinereum, the pons and the geniculate bodies seemed particularly large; the surface of the pons and the quadrigeminate tubercles were irregular; the hypophysis was large, and the pineal gland was normal in size. After fixation, the significant observations were: thickening of the septum pellucidum, widening of the fifth ventricle and relative thinning of the corpus callosum and anterior commissure. The cortical substance was increased, and the white matter seemed relatively diminished. The enormous size of the thalami, the geniculate bodies, the anterior quadrigeminate tubercles and the base of the pons was striking on coronal section. The medulla, the caudate nucleus, the putamen, the pallidum and the tegmentum of the pons were hardly larger than normal. The region of the cerebellar nuclei was voluminous. There was an area of softening in the right internal capsule.

Stains for myelin sheaths showed demyelinization only in the region of the dorsal nuclei of the thalamus, which was most marked caudally. The striatum profundum of the pons was poor in myelin, and the central tegmental tract was slightly pale. While the intrapontile portion of the fifth nerve was seen well on both sides, the peripheral and extrapial portions of this nerve were almost completely demyelinated. The optic tracts were involved, especially in their dorsolateral aspects.

Nissl preparations showed diffuse infiltration of the nervous system by cells with long, spindle-shaped nuclei, having a distinctive chromatin structure. The neural parenchyma was spared. This infiltration was most intense in the thalamus, near the third ventricle, and in the hypothalamic region. These cells were also observed in great numbers in the tangential layers of the cerebral and cerebellar cortex. They were often seen lined up along intact, myelinated nerve fibers, blood vessels and dendrites of the larger ganglion cells. They were definitely Schwann cells. Occasional mitotic divisions were noted. Satellitosis of these cells about the cell bodies of the larger ganglion cells was frequent, especially in the thalamus and the geniculate bodies. The region of the motor nuclei of the cranial nerves was relatively free from the infiltrating cells. This was also true of the anterior horn cells of the cervical portion of the cord. The marked involvement of the hypothalamic nuclei was noteworthy. The pineal gland was free from the cells. The eighth nerve, the optic tract and the fifth nerve on both sides showed diffuse neurofibromatosis. No nodules were present.

Van Gieson preparations disclosed a slight increase in the connective tissue of the leptomeninges, and hyaline changes in the walls of the small vessels in the upper layers of the cortex. The endothelium of all these blood vessels was intact. There was an increase in the fuchsinophilic connective tissue between the nerve bundles of the infiltrated eighth nerve. Bielschowsky stains showed intact axis-cylinders throughout. The macroglia seemed poorly developed. No gliosis was present, and the cytoplasm and processes of some of the Schwann cells resembled those of a spongioblastoma.

Santha denies any histogenic relation of the Schwann cells to the oligodendroglia. The poor development of the macroglia in this case, as well as the occasional transitional form between the Schwann cells and the macroglia cells, suggests a relation between the infiltrating lemmoblasts and the macroglia cells. Santha prefers to consider this case one of glioblastosis due to faulty development of glial elements, on the basis of a defective anlage. The trauma to the head also played a rôle. Only such a theory can explain the diffuse presence of these abnormal cells throughout the nervous system. Antoni explained the central neuroma as the result of failure to regress of elements of the neural crests which did not wander toward the spinal ganglia. Santha cannot accept this hypothesis, for it does not explain the anatomic observations in his case. The probable rôle of trauma to the head cannot be overlooked in this case because of the close relation of the clinical changes to the injury of the head.

SAVITSKY, New York.

Psychiatry and Psychopathology

MENTAL RETARDATION AND JUVENILE DELINQUENCY. ELEANOR GLUECK, Ment. Hyg. **19**:549 (Oct.) 1935.

The relationship between feeblemindedness and delinquency cannot be determined simply by correlating these isolated factors. It is essential to correlate many other sociologic and cultural factors with intelligence. In order to do this, Glueck analyzed the histories of one thousand juvenile delinquents who had been referred to the Judge Baker Foundation. She found that 13 per cent of the delinquent children were mentally defective, whereas only 1.5 per cent of school children from the same areas were feebleminded. This disproportion does not arise from the fact that the retarded delinquent child is more easily caught and convicted than his brighter confederate, as shown by the similarity of the figures for recidivism and the age at arrest for the intelligent and the retarded groups. In order to make a more detailed analysis, Glueck divided the group into two divisions, a normal section (intelligence quotient over 80) and an inferior section (intelligence quotient under 80). Thirty-eight per cent of the subjects fell into the second group. The influence of heredity seemed material, since mental defect was found in the families of 45 per cent of the normal and 73 per cent of the inferior group. In the subnormal group the mothers were usually younger than those in the group of normally intelligent children. Of the parents of the normal group 24 per cent were illiterate, while 41 per cent of the parents of the retarded subjects were unable to read.

The families of the group with inferior intelligence were, on the whole, more indigent than those of the other group, as 85 per cent of the former and only 73 per cent of the latter were on the "ragged edge of poverty." On the other hand, a greater proportion of the group with normal intelligence were before the court for crimes of property, while the relative positions were reversed for other offenses. At the end of the period of "treatment" in the court and clinic, 90 per cent of the group with the lower intelligence continued to be delinquent, while only 84 per cent of the subjects with normal intelligence persisted.

Glueck concludes that there are more feebleminded persons in delinquent groups than in the general population, that mental deficiency, though not a direct cause, is a potent contributing factor and that such differences of behavior as exist

between normal and retarded deliquent children arise from the mental deficiency. A knowledge of this should inspire teachers of classes of retarded children to recognize their greater responsibility to the community and should result in the more intelligent special training of such children. DAVIDSON, Newark, N. J.

ON PROJECTION. DORIAN FEIGENBAUM, Psychoanalyt. Quart. **5**:303, 1936.

There are two groups of defense mechanisms: 1. The central-passive groups, of which repression, regression, identification (introjection) and anxiety are examples. These have a predominantly centripetal tendency, operate within the ego nucleus and signify resignation. 2. The peripheral-active group, to which reaction formation and projection belong. These have a predominantly centrifugal tendency, operate at the periphery of the ego, show a high degree of aggression against the environment and are responsible for the conflicts with the environment characteristic of neurotic behavior.

Projection is the mental mechanism most commonly encountered in analytic work; i. e., it is one of the most popular methods of defense employed by the ego in its struggle against the id. Its manifestations include such apparently unrelated phenomena as superstition, ideas of reference, animistic thinking, racial prejudice, phobias, hypochondria and paranoia.

Etiologically, the following soils are favorable to the growth of projection: 1. Narcissistic fixation and regression. 2. Ambivalence of feelings. Here the repressed component of the dual affective attitude is projected. 3. Obliteration of ego boundaries. Under the increasing guidance of the reality principle, a discrete ego normally develops out of the pre-ego child-breast-mother unity. If the pleasure principle dominates over the reality principle there is more or less complete inability to achieve differentiation between the "I" and the "not I." This inability may reach such a degree that the subject's idea or sensation becomes endowed with cosmic significance. Wälder called this tendency to expand an isolated thought into a philosophic system "hypergnosis," i. e., the hypertrophied apperception of external reality. Eventually this may result in a complete breakdown of object cathexis.

The actual recourse to projection is favored by the following conditions: (1) Emergencies which bring about an inner realization that the restoration of cathexis is imperative; (2) the sense of guilt and the consequent moral code of the superego, "Not I—but they," and (3) a hypertrophied need for love.

In paranoia the unconscious, all-absorbing thirst for love is at the root of the awareness of environmental hostility.

Normal projection results from minor injuries to ego boundaries and a minor degree of weakening of the reality-testing faculty. Its outstanding manifestation is animistic thinking, the personification of natural phenomena. Dreams are often attempts to externalize internal conflicts, i. e., projection of the conflict. Imaginative literature, poetry, fiction and dramatic art are basically biographic, and therefore a form of projection. Most religious beliefs and superstitions are examples of normal projection. For example, the "evil eye" is a projection of the subject's hostility. Prejudices may be essentially a projection of repressed (displaced) aggression. The Jew's awareness of antisemitism may sometimes be based less on reality than on a projection of his unconscious antigentilism. A normal projection of greatest significance to society is the anthropomorphism of machinery; i. e., the machine is an unconscious projection of the human body—the robot idea, up to the present, being its highest form.

The effects of normal projection may be socially indifferent or beneficial, or else inhibiting or harmful only in association with other factors, sociologic or economic. The subject is not aware of the conflict underlying the normal projection, and the defensive projections lend themselves to successful rationalization. Projection becomes pathologic when it brings subjective suffering or objective irrationality.

There are two types of projection in illness—endosomatic and exosomatic. The symptoms of conversion hysteria are examples of the first. The id desire is regarded as dangerous and is displaced from the danger zone where it actually occurs and is projected onto another part of the body. It is endosomatic, for it does not pass the body boundaries. Endosomatic projection occurs also in purely depressive states. The depression is a form of delusion of persecution by the subject's conscience—a sort of introverted paranoia.

In the exosomatic type of projection the feared internal instinctual cravings are projected onto an object outside the body. It is not easy to recognize any material difference between the mechanism of projection in the phobias and that in paranoia. In paranoia the projection is at first endosomatic, for all paranoias start with hypochondria. The hypochondriacal concentration on one organ makes that part of the body exosomatic from a psychologic point of view. After this period of incubation, the exosomatic projection occurs.

Projection is the major mechanism in auditory hallucinations.

Often, close to the end of an analysis, there occurs a temporary flare-up of symptoms, with castration anxiety in the foreground, followed by a brief period of pessimism, resignation, distrust and accusativeness—all projection phenomena. This is followed by a rise of definite new plans, desires and attitudes which are healthy and directly related to reality. This occurs because the reaction formations of the neurosis have been destroyed and the striving for genitality has been successful through reforming a new ego ideal with which the normal superego does not interfere. The opposite situation happens when a psychosis occurs. The reaction formations are swept away, and the newly released instinctual desires burst out with regressive relinquishment of reality, the projection of the passive homosexuality, giving up of genitality and the establishment of a fantasy ego; i. e., the prepsychotic person resorts to projection in a final attempt at self-cure.

When a delinquent ego develops, the striving for genitality is given up, and the hostility is projected onto the world. The delinquent person finds a substitute for reality by combating it, his projections sanctioning the delinquent act.

Projection is a preferred method of defense in conditions characterized by a struggle for genitality. It is essentially a vital function the absence of which is detrimental, as is seen in schizophrenic deterioration.

PEARSON, Philadelphia.

MENTAL DISORDER ASSOCIATED WITH CHILD-BEARING. J. S. HARRIS, Brit. M. J. **1**:835 (April 25) 1936.

An analysis is presented of forty-five cases of patients admitted to a hospital for mental disease during the period from 1931 to 1934. In thirty-seven patients with mental illness first appearing during childbirth, the factor of child-bearing appeared to be the cause in whole or in part. These patients manifested one of three reactions: a manic-depressive state (fifteen), delirious reactions (eight) and schizophrenic reactions (fourteen).

In the group under consideration five patients showed symptoms during pregnancy—some as early as the fourth month and others as late as the eighth. Three patients showed psychotic symptoms immediately after the occurrence of a miscarriage. Of the remaining patients ten showed symptoms within a week after delivery; nine, during the second week, and four, in the third and fourth weeks; in the remaining four patients the time of onset ranged from the second to the eighth month after parturition. The mode of onset of the psychosis was difficult to determine exactly. In fifteen patients the symptoms appeared in well marked form within a day or two; in twenty they appeared more gradually, that is, in from several days to a few weeks. The average duration of the mental symptoms in the twenty-six patients who recovered was ten months. Nine recovered within five months, and nine, between six and seven months, and in the remaining eight patients the time ranged from eleven to thirty-three months.

When the different forms of mental disorder encountered in this series of thirty-seven cases were considered in detail by the authors, it was evident that a number of causal factors other than the child-bearing, either singly or in combination, appeared to play a part in development of the psychosis. Child-bearing, of course, played the salient rôle in all cases.

BECK, Buffalo.

THE FINAL GOAL OF PSYCHO-ANALYTIC TREATMENT. MICHAEL BÂLINT, Internat. J. Psycho-Analysis **17**:206 (April) 1936.

Psychoanalytic treatment is a natural process of development in the patient. According to Freud, the final goal of treatment is making conscious the unconscious, the removal of infantile amnesia or the overcoming of resistances. All these mean essentially the same thing. Bálint describes a case in which he analyzed after the patient had had a previous analysis of several years' duration. Although in the second analysis the patent did not bring any new material from his unconscious, he recovered from the neurosis. Consequently, some process was instrumental in recovery other than those described by Freud.

According to other authorities, the final goal of treatment is "abreacting of strangulated affects." Ferenczi and Rank described the goal as the "complete reproduction of the Oedipus relation in analytic experience." Reich described it as the attaining of full genitality, of orgastic potency. Bálint disagrees with Melanie Klein, who stressed the negative rather than the positive instincts in the child. He calls attention to real situations as the cause of the neurosis.

A person becomes ill because from childhood he has been treated with more or less lack of understanding by those around him. Gratifications were denied which were necessary to him, whereas others were forced on him which were superfluous, unimportant or even harmful. His mind, moreover, was compelled to submit to external force; it had to build up various structures, above all a superego, in order to enable him automatically to avoid conflicts with his reality. He comes to the analyst, with whom he cooperates in a study of his biologic and mental structure, and tries to bring this into connection with his conscious and primal history. Finally, he understands his own nature, and also the long and painful process through which he was formed into the man he now knows. Many persons who have been not too severely damaged in their object-relation are content with the relief which comes with consciousness, with the accompanying better control of their actions and the extended capacity for pleasure. As the work progresses, they become slowly, almost imperceptibly, healthy. With them the real end-phase of the treatment is absent or, at most, is merely indicated. With the others, however, who were obliged to suffer severely from the "confusion of tongues," whose capacity for love was wholly stunted artificially by lack of understanding in their upbringing, a peculiar situation finally arises. Everything turns on one decision. Shall one regard all past suffering as over and done with, settle accounts with the past for good and, in the last resort, try to make the best use of what possibilities there are in the life still lying ahead? This decision to begin to love really anew is far from easy. Here the analyst can help considerably. Correct interpretations are important; by them he shows that he understands the patient and will not treat him with lack of understanding, as was once the case. The most important thing here, however, is that one should take notice of the timid attempts, often only feebly indicated, toward the new beginning of the object-relation and not frighten them off.

Bálint believes that there is too much talk about constitutionally determined sadism and masochism. There should be more understanding of love impulses and less of sadism.

KASANIN, Chicago.

THE FATE OF ONE HUNDRED AND FIFTY PSYCHIATRIC OUTPATIENTS. IAN SKOTTOWE and MADELINE R. LOCKWOOD, J. Ment. Sc. **81**:502 (July) 1935.

One hundred and fifty consecutive and unselected patients were studied in a psychiatric outpatient department. Skottowe and Lockwood found that a total of 114 psychotic and psychoneurotic patients were suitable for active treatment. Of 68 unselected patients 70 per cent have recovered or are much improved. Forty-seven

per cent of the patients known to have been treated required hospitalization in institutions for mental disease. The patients who were sent to hospitals showed a recovery rate of 75 per cent. These patients showed a greater rate of recovery than those treated at home. Skottowe and Lockwood point out that the prognosis is much better for outpatients than for patients who are immediately committed to hospitals for mental diseases. Patients who come voluntarily to the outpatient department are more accessible and have better insight and better rapport with the physician. Schizophrenic patients constituted the largest group of those who refused to accept advice and treatment.

KASANIN, Chicago.

MELANCHOLIA: PROGNOSTIC STUDY AND CASE-MATERIAL. AUBREY LEWIS, J. Ment. Sc. **82**:488 (Sept.) 1936.

Sixty-one cases of depression have been collected by Lewis. Of these the condition in forty-seven was found satisfactory for analysis. The majority of the patients were women. Some had not been committed to a hospital. The ages ranged from 15 to 63 years, those of the majority of the patients being between 20 and 40. Both involutional and reactive depressions were included. Fourteen patients recovered completely, with no subsequent attacks; four recovered similarly after another attack, and nineteen were well and working but showed the neurotic traits and instability which had been present before their illness. Seven patients had subsequent attacks, and four were suffering an attack when the follow-up study was made.

Lewis finds that there are no unequivocal prognostic signs concerning the duration of the current attack or the subsequent course. One cannot point to any group of symptoms which indicate a definite direction in the prognosis. In general, retardation and stupor are favorable signs, whereas agitation, self-reproach, ideas of influencing others, voracious eating and vascular and endocrine diseases are unfavorable. The patients who died were all hopeless, self-accusatory and unresponsive to reassurance. Lewis believes that by studying the case as a whole one can make a more satisfactory prognosis than by considering one or a group of details.

KASANIN, Chicago.

PROGNOSIS OF THE DEPRESSIONS OF LATER LIFE. E. W. ANDERSON, J. Ment. Sc. **82**:559 (Sept.) 1936.

This study is limited to fifty unselected cases of women over 40. The average age was 51.5; the youngest patient was 41 and the oldest 74. Anderson attempts to determine what, precisely, are the prognostic criteria in a large group of cases of depression occurring in later life and to find some guide free from the usual ideas of such defeatable preconceptions as involutional melancholia. His general conclusion is that the prognosis in such cases of depression is on the whole poor. Roughly, a third of the total number of patients recovered completely in a reasonable time, i. e., in from one to two years; another third recovered partially; i. e., and they are able to do a little housework or to attend to simple routine tasks, the remainder either were in a hospital for mental disease or had died.

When one leaves aside the question of heredity, it is difficult to find anything of prognostic help in the previous histories of the patients. The prepsychotic personality seems to be a poor guide. Whether the existence of certain morbid personality traits is an ominous feature portending severe depressive illness in later life cannot, of course, be deduced from the present material and suggests the desirability of such a study on a large scale. It is striking that the so-called good personalities should be in such a small minority. On the whole, absurdity of ideas tends to be more frequent in conditions which will not end in recovery. It may also be noted that paranoid ideas are somewhat unfavorable.

In summing up any individual case, Anderson lays stress on: (1) hereditary burdening, especially when this is heavy; (2) the occurrence of multiple attacks; (3) hallucinations and the existence of certain symptoms, e. g., ideas of negation and, possibly, certain kindred ideas, and (4) the absurdity and bizarre nature of delusions.

KASANIN, Chicago.

ON SOME CONSTITUTIONAL ASPECTS OF CHOREA AND ON ITS SEQUELAE. E. GUTTMAN, J. Neurol. & Psychopath. **17**:16 (July) 1936.

The importance of the constitutional factor in the etiology of chorea is clearly indicated in studies of the family history and premorbid personality. In many respects, investigations on the rôle of constitution in schizophrenia yield similar results. There exists, moreover, a constitutional relationship between chorea and schizophrenia. This is noted in the frequency of catatonic psychoses in the family history of patients with chorea and in resemblances between the prechoreic and postchoreic personality and the schizoid psychopathic type. In a review of the records of Maudsley Hospital, London, Guttman finds that Sydenham's chorea is nearly twice as frequent in schizophrenic as in manic-depressive patients and that it is even more common in the history of the neuroses. It is known that in patients recovering from chorea, abnormal personality traits and disturbances in motility frequently persist. The personality deviations cannot be regarded as definite pathogenic factors in the subsequent development of the psychosis, since observations indicate an abnormal personality prior to the onset of chorea. Disturbances of motility, however, are probably definite sequelae of the chorea. These abnormal personality traits and disturbances in motility can be assumed to act as pathoplastic factors in the ensuing psychosis.

N. MALAMUD, Ann Arbor, Mich.

DEPRESSIVE PSYCHOSES OCCURRING AT THE MENOPAUSE. H. HOVEN, J. belge de neurol. et de psychiat. **36**:639 (Oct.) 1936.

Hoven believes that certain characteristics peculiar to menopausal psychoses serve to differentiate them from ordinary depressions. These are marked negativism, hysterical manifestations, childlike mannerisms and stereotypy. The evolution of the disorder, especially recovery, is often protracted. Hoven is not willing to make a definite statement as to whether the involutional melancholias constitute a specific entity which may be differentated from the manic-depressive group of disorders, but he believes that all melancholias occurring at the menopause show certain manifestations which distinguish them from the ordinary depressions.

WAGGONER, Ann Arbor, Mich.

HOMONYMOUS STATES IN PERNICIOUS ANEMIA. HERTA COSACK, Ztschr. f. d. ges. Neurol. u. Psychiat. **152**:145 (Feb.) 1935.

There is an increasing interest in the early mental symptoms in pernicious anemia. Mental changes are often present before the diagnosis is established. A man aged 44 with pernicious anemia had a severe depression, with ideas of having sinned, ideas of reference and hypochondriacal attitudes. It could not be determined from the clinical condition whether the mental condition was precipitated by the organic illness—whether it was an accidental, endogenous state or a conditioned, exogenous symptomatic psychosis. A second case is reported of a man aged 51 who had had pernicious anemia for a year and in whom there developed a manic attack, with ideas of religious grandeur and ideas of reference without disturbance of consciousness. In both cases the absence of symptoms characteristic of exogenous disease is especially clear. Both cases are striking because of the lack of heteronymous symptoms and of any special predisposition to manic-depressive psychosis.

MICHAELS, Boston.

Diseases of the Spinal Cord

OPERATIVE REMOVAL OF SPINAL CORD TUBERCULOMA. CULLEN WARD IRISH and R. B. RANEY, Bull. Los Angeles Neurol. Soc. **1**:93 (June) 1936.

A Negro aged 35 experienced painless and progressive weakness of both lower extremities, which led in two months to complete flaccid paraplegia, with anesthesia below the level of the fourth thoracic dermatome and loss of voluntary

control of the bladder. For a year prior to onset of the motor symptoms he had had night sweats and a productive cough. Six months before examination he had been hospitalized for ascites and 6,000 cc. of greenish fluid had been removed. Inoculations of guinea-pigs proved negative. During development of the paraplegia he had two generalized convulsions. Spinal puncture revealed xanthochromic fluid and complete block. At operation a small "encapsulated" intramedullary tuberculoma was removed successfully from the level of the fourth dorsal segment. The ultimate prognosis was considered poor because of the probability of development of disseminated tuberculosis.

MACKAY, Chicago.

NEOPLASMS OF THE SPINAL CORD: REVIEW OF FORTY-TWO SURGICAL CASES. R. GLEN SPURLING and FRANK H. MAYFIELD, J. A. M. A. **107**:924 (Sept. 19) 1936.

Spurling and Mayfield studied the clinical, laboratory and roentgenographic data in forty-two cases of tumor of the spinal cord in which surgical treatment was given. The percentage of benign neoplasms of the spinal cord is remarkably high, being 56 per cent in this series of cases. A benign lesion can usually be completely removed, but if recovery without disability is to be assured, the removal must be accomplished in the early stages of the disease. Tumor of the spinal cord is a relatively common lesion and should not be the last consideration in a differential diagnosis of disease of the cord. Careful analysis of symptoms, physical examination, study of the dynamics and chemical composition of the spinal fluid, roentgenographic examination of the spine and studies of the subarachnoid space with iodized oil will in every case disclose the presence and location of the lesion, even in the early stages of the disease. The importance of pain as an early symptom of tumor of the spinal cord has been overemphasized. It was an early symptom in 50 per cent of this series of patients, and 26 per cent had no pain at any time. Treatment is always surgical, except for certain malignant tumors of the vertebrae. Complete removal of a benign tumor is usually possible. A glioma of the cord can occasionally be completely removed, but in most instances one must be satisfied with subtotal removal followed by intensive irradiation. In certain gliomas even microscopic diagnosis should be dispensed with, if biopsy would incur damage to the normal substance of the cord. It is impossible to predict the degree of functional recovery from the appearance of the cord at operation. In some cords the thinness of ribbon a good return of function will be shown, while in others with only moderate indentation little recovery will follow. Every patient with some preservation of function below the level of the lesion, even though it is only an isolated reflex, will experience improvement after removal of the neoplasm.

EDITORS' ABSTRACT.

SPINAL COMPRESSION CAUSED BY ECCHONDROSIS OF THE INTERVERTEBRAL FIBROCARTILAGE. WILLIAM A. HAWK, Brain **59**:204, 1936.

One of the first references to compression of the cord by any type of chondroma is in Oppenheim's "Textbook of Nervous Diseases" (authorized translation by Alexander Bruce, ed. 5, Edinburgh, O. Schulze & Co., 1911, vol. 1), in which it is stated that Sich in 1904 removed a spinal chondroma. Middleton and Teacher (1911) and Goldthwaite (1911) recorded cases of spinal compression due to changes in the intervertebral disks. Potel and Veaudeau (1913), Delaginière (1923) and Elsberg (1925) reported cases. In 1928 Stookey presented this condition as a clinicopathologic entity, since which many cases have been reported. Schmorl and Andrae (1929) published the results of postmortem examinations made as a routine and advanced the theory of herniation of the nucleus pulposus as the underlying cause. An analysis of the literature reveals from fifty to sixty cases of chondroma, with a frequency of 14 per cent of all tumors of the spinal cord. The author considers this too high, the figure probably lying between 5 and 10 per cent.

The chondroma is firm in consistency and is bluish gray, translucent and usually encapsulated. The microscopic appearance is much like that of normal cartilage, but the arrangement is not usually as regular. In differentiation it may be impossible to separate a chondroma from normal fibrocartilage. Chondroma and the normal nucleus pulposus are easily distinguished, but differentiation between chondroma and the altered calcified nucleus pulposus is difficult.

There are two main theories regarding the etiology of this condition. The original theory is that the lesion is neoplastic; hence it is given the name "chondroma." According to a more recent theory, the lesion is a herniation of the nucleus pulposus through the annulus fibrosus, with secondary changes in the herniated tissue. Most earlier writers (Potel and Veaudeau, 1913; Elsberg, 1925, and Stookey, 1928) regarded the lesion as neoplastic. The chief points in favor of this view are the microscopic appearance and the long history, which suggests a benign, slowly growing neoplasm. In one of his later articles Elsberg (1931) admitted the possibility that the chondroma is due to hypertrophy of the disk. Alpers, Grant and Yaskin (1933) expressed definite preference for the neoplastic theory.

The more recent theory, that of herniation of the nucleus pulposus, was originally proposed by Schmorl (1929) and Andrae (1929). They showed that nodes of cartilage, single or multiple, are often observed in persons past the age of 50. These nodes have a definite communication with the nucleus pulposus and may resemble the normal or diseased nucleus pulposus which has undergone cartilaginous, calcareous or degenerative changes.

The mechanism of production of the node may be considered to be as follows: 1. The nucleus pulposus is definitely expansile and at autopsy is seen to project above the cut surface of the disk. Keyes and Gompere (1932) drilled holes through the annulus fibrosus of animals; in the animals surviving for a few weeks necropsy revealed herniation of the nucleus pulposus beneath the longitudinal ligament, producing small, nodular swellings. 2. The annulus fibrosus is thinnest and smallest in its posterior portion, and here the disk would be weakest when involved by a diffuse pathologic process. 3. The changes in the annulus are produced by trauma in a tissue which has been weakened by degenerative changes. 4. The majority of cases occur in later life, when degenerative changes in other systems are present and recognizable; pure chondroma, on the other hand, is usually observed during the adolescent period and stops growing with the cessation of general growth. 5. Herniation takes place beneath the denticulate posterior longitudinal ligament and is most pronounced in the weakest areas, namely, lateral to the midline. This explains the usual slightly lateral position of these structures. 6. The structure of the node is that of the normal nucleus pulposus or of a nucleus pulposus which has undergone degenerative and hyperplastic changes. The structure of pure nucleus pulposus is rare, the usual changes being either the laying down of a dense cartilaginous matrix, producing tissue resembling fibrocartilage, or in some cases the occurrence of areas of calcification or ossification, forming a firm, hard node.

Hawk reports ten cases of spinal compression due to ecchondrosis of the intervertebral disk. Analysis of these cases and of those reported in the literature discloses: The ages of the patients average 45 years, with a range of from 20 to 63 years. Roughly, two-thirds are males. A definite history of trauma was present in one third of the cases. The symptoms and physical signs are essentially those of spinal compression. From the point of view of differential diagnosis, the following points are in favor of a cartilage node: history of trauma preceding the illness; presence of intermittent root pains for a long period, even four or five years, before the onset of spinal symptoms; an initial onset of root pain followed by weakness and later by sphincter troubles. Neither the motor nor the sensory signs are characteristic. The spinal fluid shows no characteristic changes, but roentgenography may reveal the presence of an altered intervertebral disk or calcification of the node.

From a study of his own material, the author believes that the structure suggests origin from the nucleus pulposus, with later hyperplasia and fibrocartilaginous changes.

SALL, Philadelphia.

THE CLINICAL PICTURE OF MINOR CORD LESIONS IN ASSOCIATION WITH INJURIES OF THE CERVICAL SPINE. F. M. R. WALSHE and JEAN ROSS, Brain **59**:277, 1936.

The clinical picture resulting from the less severe injuries to the spinal cord has not been adequately described and is usually unrecognized. The spinal cord sustains relatively slight damage—either momentary nipping, when there is displacement of the cervical vertebrae in relation to one another, or momentary stretching over the posterior aspect of the vertebral bodies, when the head is forcibly flexed, as in a fall in which the vertex strikes the ground first. The original trauma may be trivial, but it acts by producing excessive flexion, anterior or lateral, of the cervical part of the spine. In the majority of such cases fracture or dislocation occurs between the fourth and the fifth or the fifth and the sixth vertebra, the latter level probably being the more common.

Six cases of minor injury to the cervical portion of the cord are reported by the authors. In only one instance had the condition been recognized; the diagnoses included those of progressive muscular atrophy, amyotrophic lateral sclerosis, primary lateral sclerosis and arthritis of the shoulder. In all six cases there was a history of primary injury to the head. Four patients were rendered transiently unconscious, and two were transiently "dazed." Thus, attention is usually not drawn immediately to the injury to the spine or cord.

The essential elements in the clinical picture are: 1. Limitation of movement of the head and neck, with pain and stiffness on movement. This was present in all cases. 2. General weakness of the upper limbs, sometimes associated with special weakness and wasting of the muscles supplied by the fifth and sixth cervical segments. This was present in two cases. Hypertonus and slowness of movements of the forearms may be present. 3. Changes in the tendon reflexes of the arms. This is perhaps the most significant diagnostic information obtained. Whereas in amyotrophic lateral sclerosis, with which injury to the cervical portion of the cord is commonly confused, the tendon jerks of the arms are uniformly and sometimes considerably increased, in traumatic conditions the tendon jerks of the arms are variably affected. Some are increased and some diminished or abolished, and one, the supinator jerk, may be replaced by flexion of the fingers. Replacement by flexion of the fingers represents inversion of the radial reflex. It is the differential behavior of the arm jerks that indicates the presence of a focal lesion of the spinal cord in the region of the fifth cervical segment, the segment usually involved in this type of spinal injury. 4. Slight hypertonus of the extensor group of muscles in the legs, with increase in knee and ankle jerks and in some cases in ankle clonus and extensor plantar responses. Slight weakness in dorsiflexion and a spastic gait may also be seen. 5. Absence of sensory loss at the time the condition comes under observation. In one case some impairment of sensory acuity to light touch and to pinprick was presented on the ulnar side of one forearm. 6. Absence of defects of sphincter control. 7. Slow and imperfect recovery.

Inversion of the radial reflex as described by Babinski (1910) has rarely been described correctly in English textbooks. Babinski stated that percussion of the inferior extremity of the radius in a normal person results in flexion of the forearm on the arm. This may be accompanied by some flexion of the fingers and the hand on the same side, but the flexion of the fingers is always less marked in extent than that of the forearm. If on percussion of the inferior portion of the radius decrease or absence of flexion of the forearm results in association with increased flexion of the corresponding fingers, this is of pathologic significance and is termed the Babinski inversion of the radial reflex.

In discussing the localizing value of this inversion, Babinski (1934) said that in a lesion of the cervical region of the cord the tendon jerks of the lower limbs are uniformly increased but that it is otherwise with the arm jerks, the form of which depends on the localization and extent of the lesion. If the lesion extends from the fifth to the eighth cervical segments, all the arm jerks may be abolished. With less extensive lesions not all the jerks may be abolished, and

inversion of the radial reflex may be seen. For this to occur three conditions are necessary: (1) There must be a lesion of the fifth cervical segment; (2) the eighth cervical segment must be intact, and (3) there must be involvement of the pyramidal tract at a level higher than the eighth cervical segment.

As a rule, inversion of the radial reflex is accompanied by increase in the triceps jerk and diminution of the pronator reflex. Pathologically, this phenomenon is most often seen in syringomyelia and in association with a traumatic lesion and compression of the cervical portion of the cord. SALL, Philadelphia.

ABSCESS OF THE SPINAL CORD. R. MILNER WALKER and S. C. DYKE, Lancet **1**:1413 (June 20) 1936.

Woltman and Adson (1926) found only twenty-nine cases of abscess of the spinal cord in the entire literature. The commonest causes of this abscess are injury or disease of the spine and chronic inflammatory disease of the lungs. In only two cases was recovery recorded; in both the abscess was drained by operation. In one instance the condition was associated with fracture of the spine, and permanent paraplegia persisted. The patient reported on by Woltman and Adson, in whom the abscess resulted apparently from suppuration at the site of preexisting acute myelitis, made a complete functional recovery.

Walker and Dyke report a case of abscess of the spinal cord in a child 3 years of age, who recovered after operation. The child entered the hospital in October 1934 with a history of attacks of headache and vomiting for twelve months. During these attacks she lost the use of her legs, and the mother stated that she screamed with pain when the perambulator was wheeled over rough stones. Between attacks she was able to walk well. During the week before entering the hospital, headache had been more severe and persistent; vomiting had occurred daily, and the child had lost the use of her legs. On her admission the temperature was 101.4 F., the pulse rate 140 and the respiratory rate 32. There were rigidity of the neck and a Kernig sign. Both lower extremities were spastic, with increased tendon reflexes and a Babinski sign bilaterally. The reflexes in the upper extremities were normal. The spinal fluid contained pus and pneumococci. Subsequently, it was observed that the patient had spina bifida, involving the fourth and fifth lumbar vertebrae. At a second lumbar puncture 10 cc. of foul-smelling, frankly purulent fluid was first obtained. As the needle was being withdrawn, another 4 cc. of fluid of quite different appearance flowed from it. The chloride content differed in the two specimens of fluid, indicating the presence of a localized collection of purulent fluid. Laminectomy was performed, including the third, fourth and fifth lumbar laminae; the dura was thickened and red; when the dura was incised, a small amount of turbid cerebrospinal fluid escaped but no pus was seen. The patient was operated on again about three weeks later; when the dura was opened, the spinal cord appeared swollen and congested; when the cord was incised, 12 cc. of thick pus escaped. The patient improved gradually; in April 1936 she had no headches, could enjoy playing with other children and was mentally normal for her age.

WATTS, Washington, D. C.

SYNDROME OF THE EPICONUS OF MINOR. V. BAKHTIAROFF and N. SCHIBANOFF, Arch. internat. de neurol. **54**:461 (Nov.) 1935.

The portion of the cord between the fourth lumbar and the third sacral root constitutes the epiconus, which merges at the third sacral segment with the conus medullaris. The epiconus is enveloped by the cauda equina, and a lesion of the first is likely to affect the cauda. Cases of a pure, isolated lesion of the epiconus are rare; to establish this localization it is necessary to find normal knee jerks (placing the lesion below the fourth lumbar segment) and preservation of sphincteric function (placing the lesion above the fourth sacral segment) with clinical evidence of implication of the intervening segments. The most frequent cause of damage to the epiconus is trauma—bullet wounds and falls being

the commoner types of injury. In rare cases syphilis or poliomyelitis may produce the picture. The syndrome is made up of paralysis of the gluteal and peroneal muscles, preservation of sphincteric function, absence of the achilles reflex and normal knee jerks. Bakhtiaroff and Schibanoff report the case of the symptom complex of the epiconus in a man who was injured in a fall, sustaining fracture of the pubic bone. They suggest that the condition be designated as Minor's syndrome, in recognition of Minor's classic description of the lesion in 1901.

DAVIDSON, Newark, N. J.

Peripheral and Cranial Nerves

FOLLOW-UP STUDY OF THIRTY-FIVE CASES OF PARALYSIS CAUSED BY ADULTERATED JAMAICA-GINGER EXTRACT. M. L. WEBER, M. Bull. Vet. Admin. **13**:228 (Jan.) 1937.

Weber bases his study on thirty-five cases of paralysis in ex-service men from 28 to 54 years of age at the time of onset of the paralysis, early in 1930, as the result of drinking adulterated jamaica ginger. Twenty-two of the total number were examined personally by Weber during June and July 1936, and the remaining thirteen by other physicians during the last two years. In Weber's opinion the orthopedic and neurologic residual signs, as seen in the material studied, are due solely to the original paralysis, even though four of the patients are known to have systemic syphilis and several others have continued to consume alcoholic beverages. The absence of involvement of the cranial nerves and the practical absence of mental manifestations preclude the diagnosis of either neurosyphilis or alcoholic polyneuritis. The early (1930) prognosticated restoration of motor power in the paralyzed limbs has not materialized in a considerable number of cases. The residual signs were contractures, equinovarus, bilateral foot drop, wrist drop, steppage gait, atrophy of the legs, atrophy of the hands, exaggerated knee jerks and ankle, knee and patellar clonus. Four patients were unable to stand or walk. The greater disability of the legs, compared with that of the hands, is accounted for by the fact that the neurons of the legs are longer, requiring more time for their regeneration. The pathologic changes involved appear to be combined degeneration of the lower and upper motor neurons: neuronitis of the peripheral motor nerves and anterior horn cells, in addition to the lateral motor columns of the spinal cord. The prognosis for improvement, barring orthopedic and neurosurgical intervention, appears to be grave. That the age of the patient had any influence on the outcome of the disease was not observed. As nearly all the peripheral nerves (except some of the cranial) carry both motor and sensory fibers, it is curious that so little of sensation was impaired, even in cases of the most severe involvement. It is also curious that the toxin should strike at the same time the lower and the upper motor neurons—phylogenetically the old and the new parts of the motor system.

EDITOR'S ASTRACT. [J. A. M. A.]

A CLINICAL AND ELECTRICAL STUDY OF A CASE OF PARTIAL HEREDITARY AND FAMILIAL FACIAL DIPLEGIA. R. HUMBERT and R. ROSSANO, Ann. d'ocul. **173**: 369 (May) 1936.

Humbert and Rossano believe that bilateral facial paralysis, or congenital peripheral facial diplegia, is caused by agenesis of the facial nuclei. Bilateral agenesis of the petrous portion of the temporal bone is not likely to occur, and, according to Cabannes, cases of congenital peripheral facial paralysis are extremely rare. However, recently Alajouanine, Huc and Gopcévitch reported that a congenital syndrome characterized by clubfoot, bilateral facial paralysis and bilateral paralysis of the sixth nerve occurred in four children.

Incomplete, dissociated facial diplegia, which was not only congenital but familial and hereditary, was observed in a young man on whom operation was to be performed for bilateral ptosis. The face was expressionless, with almost

complete absence of mimicry. Voluntary motility of the face was dissociated. Certain muscles (those of the cheek, lips, chin and nose) responded normally; others (the orbicularis, frontal and superciliary muscles) responded with difficulty and incompletely, while the dilator muscle of the ala of the nose did not respond. The motility reflex, which was studied principally in the region of the orbicularis muscle, was decreased, or even absent, when certain blinking reflexes were tested. There was complete absence of contraction of the elevator muscles of the eyelids. Electric and chronaximetric examination showed the impossibility of dissociating the palpebral and orbital fibers from the orbicularis muscle. Above all, examination illustrated that there were marked disturbance of chronaxia of the facial muscles and a manifest tendency to equalize these chronaxias, which was marked in the region of the orbicularis muscle of the eyelids. The two fibers to this muscle remained distinct and retained their normal chronaxias. Except for the disturbances of facial motility, there was no morphologic or pathologic change. This incomplete bilateral facial diplegia was present in five members of the same family, belonging to three successive generations.

Humbert and Rossano believe that there is need for further clinical and chronaximetric observations of this type.

BERENS, New York.

HERPES ZOSTER OPHTHALMICUS PRECEDED BY OCULAR SYMPTOMS. BUSSY and BONAMOUR, Ann. d'ocul. **173**:477 (June) 1936.

Bussy and Bonamour report the case of a child aged 7½ years who had had interstitial keratitis with folds in Descemet's membrane. These ocular disturbances were observed several days before the appearance of herpes zoster ophthalmicus in the area supplied by the nasal and infra-orbital nerves.

BERENS, New York.

MUSCULAR HYPERTROPHY AND MUSCLE CRAMPS IN A CASE OF POLYRADICULITIS. K. VON SÁNTHA, Deutsche Ztschr. f. Nervenh. **141**:249, 1936.

Von Sántha reports a case of polyradiculitis following an infectious disease which resembled influenza. The presenting features were paralysis of the left leg, with partly flaccid, partly myotonic muscle groups. The myotonic muscle groups, particularly those of the calf, showed genuine hypertrophy of the muscle fibers, verified by biopsy. These muscle groups showed painful cramps, and in the free intervals, constant myokymic fibrillation. The musculature of the whole body showed a general increase in mechanical and electrical irritability. The spinal fluid showed a high protein content (of 104 mg. per hundred cubic centimeters) and 54 lymphocytes, with dark xanthochromia. Roentgen studies showed a block at the level of from the eighth to the tenth dorsal segment, which was diagnosed as the result of arachnoid adhesions. Therefore the original diagnosis of polyneuritis was changed to polyradiculitis. Studies of the metabolism and the blood chemistry showed changes, the most noteworthy of which were conconsiderable increase in the urea content of the blood and hypoglycemia. It is thought that these changes were due to the change in the status of the musculature.

HOEFER, Boston.

POLYRADICULOGANGLIONITIS OF LANDRY'S TYPE IN A SYPHILITIC PATIENT. A. JUBA and A. SZATMÁRI, Deutsche Ztschr. f. Nervenh. **142**:28, 1937.

The authors report a case of ascending polyneuritis with involvement of the spinal roots. A vague, possibly septic, febrile disease occurred about two months before the onset of the neurologic symptoms, which persisted for two weeks. Serologic tests of the blood and spinal fluid gave strongly positive results; examination of the spinal fluid revealed 29 cells and a total protein content of 38 mg. per hundred cubic centimeters. Histologic examination showed inflammatory infiltrative changes of the spinal ganglia, roots and peripheral nerves of the lumbar region. No other changes were seen. The relation between polyneuritis and the serologic manifestations of syphilis is questionable.

HOEFER, Boston.

Cerebrospinal Fluid

ON DIFFERENTIATION OF COLORED CEREBROSPINAL FLUIDS. F. H. ROBINSON and B. N. MILLER, Am. J. M. Sc. **191**:538 (April) 1936.

Yellow spinal fluid may be due to protein, as in cases of compression of the cord, or to blood, as in hemorrhage into the neuraxis. To distinguish between these two causes, Robinson and Miller suggest the application of the benzidine test, which, they find, detects blood up to a dilution of 1:50,000. By producing compression of the spinal cord in dogs they secured xanthochromic fluid which invariably gave a negative reaction to the benzidine test; if there was any blood, up to a dilution of 1:50,000, the reaction was positive. This was true, regardless of the source of the blood—whether from trauma produced by puncture, inflammatory response or subarachnoid bleeding. To determine whether the blood is due to bruising produced by the lumbar puncture needle, they suggest centrifugation of the specimen at high speed. If the blood is from this source it will be thrown to the bottom of the tube, leaving a supernatant fluid that gives a negative response to the benzidine test.

DAVIDSON, Newark, N. J.

THE EFFECT OF THE INJECTION OF CERTAIN NITROGEN-CONTAINING COMPOUNDS INTO THE CISTERNA MAGNA ON THE BLOOD PRESSURE OF DOGS. H. RESNICK JR. and M. F. MASON, Am. J. M. Sc. **192**:520 (Oct.) 1936.

The effects of intracisternal injection of nitrogenous "retention" products into dogs were studied. Urea (in solutions of strengths up to one-half molar) and creatinine (from 250 and 500 millimols per liter) did not increase the blood pressure. Sodium urate (6 millimols per liter) and ammonium chloride produced inconstant results. Saturated solutions of cystine, cysteine hydrochloride and tyrosine gave negative results. Aspartic acid (30 millimols per liter) and glutamic acid (50 millimols per liter) gave inconstant effects. The injection of calcium salts lowered the blood pressure, which had been previously increased by glutamic acid. Intracisternal injections of as little as 0.2 mg. of methyl guanidine sulfate per kilogram of body weight caused a pronounced rise in blood pressure. Guanidine hydrochloride caused a rise in blood pressure; both guanidine compounds also resulted in muscular twitchings. Intracisternal injection of calcium salts diminished the blood pressure and controlled the muscular twitchings previously induced by guanidine. In these experiments the action of guanidine was central rather than peripheral.

MICHAELS, Boston.

CLINICAL STUDIES IN POST-LUMBAR PUNCTURE HEADACHES. T. J. HELDT and LESTON S. WHITEHEAD, Am. J. Psychiat. **93**:639 (Nov.) 1936.

The incidence of headache following puncture is estimated to be about 23 per cent. The complication is probably associated with the effects of negative pressure in the epidural space. This headache, in its severe and disabling form, may be prevented in most cases by inserting into the puncture hole a strand of sterile, anhydrous catgut. This promptly becomes swollen, effectively plugging the hole. The patient rests for about ten minutes after the tap and then may be up and about. A 19 gage needle with a Pitkin point should be used, and it is necessary to have a small adapter and a specially marked stylet. The adapter is pushed into the hub of the needle after fluid has been withdrawn, and then catgut is inserted with the stylet until it reaches the point marked on the stylet which indicates that its outer end is at the plane of the adapter. The needle is then pulled out quickly along a supporter, while the catgut is advanced. In most patients a mild reaction to catgut, consisting of backache and dull headache, may be expected; but it is much less severe and disabling than the usual headache following puncture.

DAVIDSON, Newark, N. J.

COMPARATIVE STUDIES ON DIASTASE IN SERUM AND SPINAL FLUID. H. CHRISTIANSEN, Acta psychiat. et neurol. **11**:195, 1936.

Christiansen undertook to investigate the relationship between the diastase content of the blood serum and that of the spinal fluid. He used the method for the determination of diastase in the serum given by Nörby (1931). The amount of diastase present in the spinal fluid is so small that it is necessary to use undiluted fluid and a much longer reaction time (up to five hours) than that for serum. In order to have easily surveyable figures and because the amounts of diastase in the spinal fluid are too small, he found it expedient to express these values by the reaction constant multiplied by 10. Care was taken to use spinal fluid free from red cells, so as to exclude this source of error. Studies were made in nine cases of dementia paralytica, ten of dementia praecox, four of encephalitis, seven of epilepsy, nine of constitutional psychopathy, nine of manic-depressive psychosis, nine of chronic alcoholism and forty-nine of various neuropsychiatric disorders. This material was supplemented by a group of twenty-seven surgical cases. Values from 4 to 7 were found in 71 per cent of the cases; below 4, in 15 per cent, and above 7 (from 8 to 11), in 15 per cent. Values above 11 were found in less than 1 per cent of cases. When he expressed the diastase values for spinal fluid in percentages of those for serum, Christiansen found that in 51 per cent of cases the diastase value for the spinal fluid was from 1 to 2 per cent of that for serum. In 28 per cent of the cases the ratio was from 2 to 5 per cent; in 15 per cent, from 0.5 to 1 per cent, and in about 6 per cent less than 0.5 per cent. In order to ascertain the possible rôle of the cell count of the spinal fluid in the values for diastase, the diastase content of the spinal fluid was determined in nineteen cases of acute meningitis of various types. In this group the blood serum was not available for study. The results obtained tend to show that there is no relationship between the diastase content and the cell count of the spinal fluid. The author points out that since no glandular structure which produces diastase is known in the central nervous system, it is not likely that the diastase of the spinal fluid is an "intramural" product. It is more probable that the diastase passes from the blood into the spinal fluid through the choroid plexus.

YAKOVLEV, Waltham, Mass.

Treatment, Neurosurgery

EFFECT OF ARTIFICIAL FEVER ON THE CLINICAL MANIFESTATIONS OF SYPHILIS AND THE TREPONEMA PALLIDUM. CLARENCE A. NEYMANN, Am. J. Psychiat. **93**:517 (Nov.) 1936.

Neymann recommends the use of electromagnetic induction of fever in patients placed in an air-conditioned cabinet. In 754 reported cases of dementia paralytica in which treatment with electropyrexia was employed, he finds that 2.5 per cent of the patients died as a result of the treatment; the condition of 34.5 per cent remained stationary and that of 35 per cent was improved, and 28 per cent had complete remissions. This is better than the record for malariotherapy, in which the proportion of patients who improve is about 30 per cent and in which the death rate varies from 10 to 30 per cent. In treatment for tabes dorsalis electropyrexia effected some improvement in 54 of 90 cases reported.

The effect of fever therapy has been ascribed to increase in the cell count of the blood, to dilatation of capillaries and to greater speed of the blood flow, as well as to many other physiologic factors. Neymann, however, is inclined to credit the improvement to the spirocheticidal effect of the heat. He submitted patients with primary syphilis to artificial fever, examining the serum from the chancre. The treponemes always disappeared from the chancre after exposure of the patient for two hours to temperatures in excess of 105.8 F. (41 C.). Clinically, however, it is considered advisable to supplement electropyrexia with treatment with tryparsamide and bismuth.

DAVIDSON, Newark, N. J.

THE TREATMENT OF PITUITARY INFANTILISM WITH ANTERIOR PITUITARY EXTRACT. MAX M. GOLDBERG, Endocrinology **20**:854 (Nov.) 1936.

Goldberg reports the results in a case of pituitary infantilism of the Levi-Lorain type in which treatment with anterior pituitary extract was employed. A youth aged 18½ years showed symptoms typical of infantilism, including small stature, the facial appearance of an old man (progeria), a girlish voice and lack of axillary and pubic hair. The height of the patient at the beginning of treatment was 59.4 inches (150.9 cm.), the span 52.5 inches (133.4 cm.) and the weight 79 pounds (35.8 Kg.). After the administration of anterior pituitary extract subcutaneously three times a week, over a period of four and a half months, the patient exhibited a gain in height of 2 inches (5 cm.) and an increase in weight of 6½ pounds (2.9 Kg.) and showed great stimulation of the primary and secondary sexual characteristics.

PALMER, Philadelphia.

SURGICAL TREATMENT OF MENINGITIS OF OTITIC AND NASAL ORIGIN. G. E. SHAMBAUGH JR., J. A. M. A. **108**:696 (Feb. 27) 1937.

During the last four years Shambaugh Jr. observed eight cases of meningitis of otitic or nasal sinus origin in practice or in the house service of the Presbyterian Hospital. Two patients died of sepsis (one of thrombosis of the lateral sinus and the other of thrombosis of the superior sagittal sinus), and one patient, of duodenal hemorrhage. The meningitis in these three cases was localized and was not the immediate or the contributory cause of death. The remaining five patients with meningitis were treated successfully according to accepted principles. These principles consist in the earliest possible diagnosis of meningitis by examination of the spinal fluid at the first suspicion of meningeal invasion, the cell count being the important consideration. A sharp differentiation must be made between localized meningitis, with an increased number of cells but no organisms on smear or culture and with a normal sugar content, and generalized meningitis, with organisms on smear and culture and with diminution or absence of sugar in the spinal fluid. As long as the meningitis is localized, treatment should be confined to thorough surgical drainage of the focus in the ear or sinus. Occasionally a few organisms may be observed on smear but not on culture, and here also simple drainage of the suppurative focus may suffice to produce a cure. The prognosis in localized meningitis is good if the disease is recognized promptly and dealt with. Once generalized meningitis has developed, incision and drainage of the dura at or near the point of entry of the infection may be considered; forced drainage of spinal fluid by the method of Kubie may be employed; the intracarotid administration of antiseptics may be tried, or simply repeated lumbar punctures may be relied on. While the prognosis for generalized meningitis of otitic or nasal sinus origin is usually poor, occasional recovery does occur, especially in meningitis due to the streptococcus.

EDITOR'S ABSTRACT.

THE PSYCHOPATHOLOGY AND TREATMENT OF THE PARKINSONIAN SYNDROME AND OTHER POST-ENCEPHALITIC SEQUELAE. WALLACE MARSHALL, J. Nerv. & Ment. Dis. **84**:27 (July) 1936.

Marshall selected from the clinic a group of reasonably intelligent patients with the parkinsonian syndrome for treatment by means of psychotherapy, relaxation and reeducation. Moving pictures of some of the patients were taken. Psychoneurotic symptoms develop, according to Marshall, as an outgrowth of the inability to coordinate and are, like those of frustration, exemplified by speech defects and behavior problems. The therapy employed was attempted relaxation of the contracted parts. Continued reassurance and effort on the part of the attendant convinced many patients of their ability to execute the exercises. Improved patients were allowed to talk to beginners, to encourage them. Emotional conflicts were discovered as far as possible, and an attempt was made to

secure a better mental attitude. Reeducational measures consisted in instruction in the reestablishment of associated movements. The patient watched a normal gait and was told to take a long, even stride, with the arms relaxed at the side of his body. Festination could be halted at the physician's command. The helpfulness of the treatment was attributed chiefly to "mental catharsis."

HART, New York.

ON THE RESPONSE OF SCHIZOPHRENIC SUBJECTS TO HYPOGLYCEMIC INSULIN SHOCK. JOSEPH WORTIS, J. Nerv. & Ment. Dis. **85**:497 (Nov.) 1936.

At the Pötzl Clinic, Vienna, Sakel has treated with insulin seventy-five patients with schizophrenia. No definite principle of dosage has yet been found. The procedure is complicated and dangerous, and two deaths have already occurred. Patients are treated with regular series of hypoglycemic shocks produced by deep intramuscular injections of insulin, varying from 20 to 200 units. The shock lasts several hours, but the response varies with the individual patient.

Constant attendance is necessary after every large dose of insulin. The pulse and blood pressure must be constantly controlled to detect early circulatory failure. Ampules of 33 per cent solution of a sugar for intravenous administration and epinephrine are kept handy, together with an apparatus for tube feeding. Hypoglycemia is ordinarily not prolonged beyond six hours, because of the danger of irreversible changes. The main point in the treatment is to know when to end the shock. It should not be terminated during excitement. Collapse, irregular pulse, marked bradycardia, marked fluctuations in the pulse rate, laryngospasm, tonic cramps, epileptic seizures, disturbances in respiration, such as the Cheyne-Stokes type or stertorous breathing, are all indications for the termination of shock. The average treatment lasts two or three months. The material is selected, preference being given to strong young persons with conditions of recent onset.

HART, New York.

HYPERTENSION PRODUCED WITH BENZEDRINE. S. A. PEOPLES and E. GUTTMAN, Lancet **1**:1107 (May 16) 1936.

Peoples and Guttman have studied the effect of artificially altering the blood pressure on normal and mentally abnormal persons. Benzedrine was given orally in doses of from 10 to 80 mg. In each subject the normal daily fluctuation of blood pressure was recorded, and the mental state was carefully considered. In this group there were only two persons who did not show any reaction to the doses used. The lowest dose to which any patient reacted appreciably was 20 mg. Twenty-two of the patients reacted to 30 mg. The latent period after oral administration of the drug generally was between forty-five minutes and two hours. The alterations in blood pressure were used as an index of the course and intensity of intoxication. The pressure changes were chiefly systolic, the diastolic showing little or no increase, so that there was increase of the pulse pressure. The systolic pressure increased from 10 to 40 mm. of mercury. Almost every patient showed an increased tendency to talk, but the effect was most striking in defective patients. They overcame their retardation, and several talked spontaneously to other persons for the first time since admission. This improvement was also visible in the patient's movements. Some of the normal patients showed motor restlessness. In no instance was anxiety produced or depression deepened, but the change was generally in the direction of euphoria. A majority of the patients complained of disturbance of sleep on the night after the experiments.

WATTS, Washington, D. C.

TREATMENT WITH ACETYLCHOLINE FOR CERTAIN CHARACTER CHANGES IN CHILDREN WITH TENDENCY TO IMPULSIVE BEHAVIOR. J. DUBLINEAU and DORÉMIEUX, Ann. méd.-psychol. **94**:99 (June) 1936.

Several authors have observed a favorable effect from the use of acetylcholine in epilepsy. The frequency of the seizures decreases and in some instances there

is improvement in the epileptic disturbance. This induced Dublineau and Doré-mieux to use acetylcholine in the treatment of delinquent children with personality changes characterized especially by impulsive behavior—temper tantrums, violence and chronic disobedience. They report four cases in which the daily injection of from 5 to 10 cg. of acetylcholine associated with the administration of phenobarbital by mouth was followed by definite improvement in behavior, with diminution or disappearance of the impulsive tendency. The improvement was noted soon after the beginning of the treatment. It was temporary, however, was effective only during treatment and rarely lasted more than a few weeks. The treatment had no untoward effects and was well tolerated.

YAKOVLEV, Waltham, Mass.

IS RESECTION OF SPLANCHNIC NERVES JUSTIFIED IN TREATMENT OF PERMANENT ESSENTIAL ARTERIAL HYPERTENSION? H. HERMANN and L. SABADINI, Presse méd. **45**:41 (Jan. 9) 1937.

Hermann and Sabadini state that most methods advocated for the treatment of permanent essential hypertension are difficult of execution and that, for this reason, they have limited themselves to resection of the splanchnic and sympathetic nerves. Essential hypertension may be permanent or paroxysmal. Paroxysmal hypertension is often accompanied by a tumor of the adrenal medulla having the characteristics of a benign adenoma. This tumor is at times juxta-adrenal, of a paraganglionic type. This is natural when the sympathetic origin of the adrenal medulla is considered. Both the sympathetic ganglia and the medulla are derived from the ectoderm. The current surgical practice is complete adrenalectomy. Quite different is the case in permanent essential hypertension, in which the lesion is much less constant. The hypertrophic gland shows medullary hyperplasia and increased hormonic contents. It is much too hazardous to assail the gland directly. It is more advantageous to dry out the secretion either by denervation or by devascularization, or, better, by resecting its secretory nerve, the splanchnic nerve. The last method is superior because it cuts the vasoconstrictor nerves, thus producing vasodilatation. The most frequently employed method is the posterior, laterovertebral, subserous (subpleural or subperitoneal) approach. It may be high or low central. Pende has recommended anesthesia of the nerve with procaine hydrochloride in hypertension crises, to be followed, in patients not fit for operation by unilateral or bilateral alcoholization of the nerve. The splanchnic nerve, however, does not alone innervate the adrenal capsule. There are posterior filaments emanating from the terminal trifurcation of the nerve and from the adrenal ganglion. It also receives branches from the diaphragmatic, renal and solar plexuses. Besides, there are often anastomoses between the right and the left splanchnic nerve. All this shows a multiplicity of origins, but only in man. In the dog, every adrenal gland receives its secretory nerves solely from the homolateral splanchnic nerve. All these, as well as the physiologic and clinical consideration, lead the authors to the realization that the pathogenesis of permanent essential hypertension is not sufficiently known to justify conclusions as to its surgical treatment. The facts given by the authors seem to be in accord with certain therapeutic results. In order to confirm them further, however, stricter scientific observations are suggested. In only a few cases has splanchnicectomy greatly improved a state of hypertension which has resisted all other treatment. They especially underscore the fact that the main body of the splanchnic nerve consists of centrifugal and centripetal conductor fibers. On cutting them one interrupts not only the vasoconstrictor and adrenal secretory fibers but also the sensitive paths used by the reflexes originating in the abdominal viscera.

EDITOR'S ABSTRACT. [J. A. M. A.]

MALARIOTHERAPY AFTER ACUTE PARALYTIC STAGE IN EPIDEMIC POLIOMYELITIS. O. KAUDERS, Med. Klin. **32**:1766 (Dec. 24) 1936.

In an epidemic of poliomyelitis, Kauders observed an unusually large percentage of adult patients and points out that for these patients the prognosis is usually less favorable than for children and young persons. In the surviving patients with paralysis, monoplegias were rare, the majority having extensive forms of paralysis. Most frequent was complete paralysis of the lower extremities, frequently with involvement of the abdominal and pelvic muscles. Treatment of the acute stage of poliomyelitis consisted generally in the administration of convalescent serum that had been obtained in this epidemic. After the acute stage the paralytic parts of the organism were subjected to intensive after-treatment in the form of massage, electrical treatment, passive and active exercises, diathermy and so on. As these measures proved ineffective in many cases of severe paralysis, the author decided to try malariotherapy. After citing the factors that induced him to resort to this measure, he gives a tabular report of eighteen cases. The table indicates that the number of malarial attacks varied from four to ten. The time of the beginning of the malarial treatment varied from sixteen to one hundred and three days after onset of the disease. In discussing the results of the treatment, the author points out that the time is too short to permit a final evaluation but that the tabular report indicates that all patients were somewhat improved and that in five cases the results were excellent. He concludes that malariotherapy is an important therapeutic aid in the paralytic sequels of poliomyelitis.

EDITOR'S ABSTRACT. [J. A. M. A.]

PROSTIGMIN TREATMENT FOR MYASTHENIA GRAVIS. M. E. SCHNEIDER, Monatschr. f. Psychiat. u. Neurol. **94**:123 (Oct.) 1936.

Schneider has used prostigmin (the dimethylcarbamic ester of 3-hydroxyphenyl trimethylammonium methylsulfate) in treating thirteen patients with myasthenia gravis. After a preliminary subcutaneous injection of prostigmin, to which all patients responded favorably within twenty minutes, oral doses of from 4 to 6 tablets, each containing 15 mg. of the drug, were given daily. All patients showed improvement. Untoward symptoms were noted on two occasions only; in one patient frequent bowel movements occurred during the first day of treatment, and another showed sweating during the first two nights, with moderate lacrimation on the following days. Schneider reports four cases in which the patients had had severe clinical symptoms. These patients, who had been observed for from two to three months, experienced almost complete relief from the symptoms and were able to resume their previous occupations.

ROTHSCHILD, Foxborough, Mass.

EFFECT OF HYPERTONIC SOLUTION OF DEXTROSE IN CASES OF ACUTE CONFUSION AND AGITATION. STEN OLDBERG, Upsala läkaref. förh. **52**:257 (Dec.) 1936.

Oldberg reports the results of treatment with a hypertonic solution of dextrose in six cases of dementia praecox in which so-called acute swelling of the brain occurred. The first patient became acutely ill and was brought to the hospital in a state of confusion and agitation. After the intravenous administration of 20 cc. of a 10 per cent solution of dextrose the patient fell asleep. The next day he was given 10 cc. of a 40 per cent solution, after which he became clearer mentally. He was treated with the same solution during subsequent days, with variable results. About three months after his admission he began to hallucinate and to express delusional ideas. The other five cases are described only briefly. Treatment in these cases had a sedative and hypnotic effect, especially if large quantities of the solution were given. Oldberg dismisses the possibility of a psychologic effect, pointing out that the patients were in a mental state which precluded psychic influence. He emphasizes particularly the hypnotic effect of the solution of dextrose.

NOTKIN, Poughkeepsie, N. Y.

Special Senses

CONGENITAL HEAD-NODDING AND NYSTAGMUS. RONALD A. COX, Arch. Ophth. **15**:1032 (June) 1936.

Two conditions have as their most prominent, if not the only, symptoms head-nodding and nystagmus: The first is acquired head-nodding and nystagmus, or spasmus nutans, and the second, congenital head-nodding and nystagmus, which may occur in several members of the same family. The differential diagnosis, according to Cox, is as follows:

SPASMUS NUTANS	CONGENITAL HEAD-NODDING AND NYSTAGMUS
1. The onset usually occurs between the fourth and twelfth month after birth, occasionally as early as six weeks after birth and sometimes as late as the third year.	1. The onset is at birth.
2. Recovery invariably takes place; the signs disappear usually before the end of the third year.	2. The condition persists throughout life.
3. No relation is found between the type of head movements and the type of nystagmus; the head movements are slow, inconstant and variable in range, and the eye movements are rapid, constant and of small and steady range.	3. The head movements seem to compensate for the eye movements.
4. The head-nodding precedes the onset of the nystagmus by from one half to two months.	4. The onset of the head-nodding and that of the nystagmus are simultaneous.
5. Spasmus nutans is occasionally monocular.	5. The congenital condition is always bilateral.
6. The media are clear; the fundi appear normal.	6. The media are clear; the fundi appear normal.

Other conditions, such as multiple sclerosis, Friedreich's ataxia and Parkinson's disease, which have among their signs head-nodding and nystagmus, can be differentiated and eliminated by other general and neurologic manifestations.

SPAETH, Philadelphia.

TRANSITORY WORD BLINDNESS ASSOCIATED WITH RIGHT HOMONYMOUS HEMIANOPIA. HARALD G. A. GJESSING, Arch. Ophth. **16**:5 (July) 1936.

Dyslexia, or word blindness, is present congenitally in about 1 per cent of all persons and is characterized by disproportion between the intellectual development of the child and the reading ability. There may be a total lack of comprehension of the reading matter. The subject frequently reverses the order of letters or words or may fail to understand certain words. These difficulties may be more pronounced when the child is trying to read fast. Such children are often considered by teachers as obstinate or inattentive.

Acquired dyslexia is also made manifest by the inability of the patient to understand written or printed language, even though vision is good. As a rule, the patient can understand spoken language without difficulty. Word blindness may be partial, so that the patient may retain, for example, the ability to read written but not printed words, or figures but not letters. The onset of acquired dyslexia may be sudden. The etiology is diverse, but the pathologic changes are localized in the posterior portion of the outer, upper surface of the angular gyrus of the temporal lobe and in contiguous portions of the occipital lobe. The

lesion often gives rise to contralateral homonymous hemianopia as well. In a pronouncedly left-handed person, disease localized to the right gyrus angularis, ceteris paribus, will give rise to a corresponding condition—left homonymous hemianopia. If the patient states that he is left handed and yet acquires right homonymous hemianopia, it is reasonable to believe that he is not entirely left handed by nature.

The case described is of interest not only from an ophthalmologic but from a psychologic point of view. A man aged 65, apparently healthy and strong, first noted his condition on reading a letter which he had dictated to a stenographer. He was astonished to find that it contained numerous invectives. When the latter was read aloud to him by the stenographer, however, it sounded precisely as he had dictated it. The patient, immediately aware that something was wrong with his mental processes, tried to find certain well known names in the telephone directory. Some of these he could find and others he could not. His general health had always been good except that for the past year he had had symptoms of prostatic hypertrophy. For these he was undergoing a series of roentgen treatments. He was left handed. The fields of vision showed right homonymous hemianopia, more marked in the left eye. Further examination and observation continued for two months. At that time the patient died of cancer of the prostate. Some time before death, however, he could read faultlessly, and the right homonymous hemianopia had disappeared wholly from the left eye and was considerably improved in the right.

SPAETH, Philadelphia.

TRAUMATIC LESIONS OF THE OPTIC CHIASMA. H. M. TRAQUAIR, NORMAN M. DOTT and W. RITCHIE RUSSELL, Brain **58**:398, 1935.

Damage to the optic chiasm, as evidenced by the occurrence of temporal defects in both visual fields, is an uncommon complication of injury to the head. A careful survey of the literature revealed only twenty-seven acceptable cases, to which the authors add three more. Cases of complete blindness of one eye and temporal hemianopia in the other are included in their study, on the basis that the most probable damage is to the optic chiasm and one optic nerve.

Analysis of the thirty cases reveals that in most cases the main injury was to the frontal region and in a few to the temporal or parietal region; a fall from a height was the commonest cause of injury. The following symptoms were presented: unilateral paralysis of the sixth nerve (seven cases), partial or complete unilateral paralysis of the third nerve (seven cases), damage of both the third and the sixth nerve (one case), loss of olfaction, impairment of hearing on one side associated with bleeding from the affected ear, facial paralysis, polyuria, progressive adiposity, Wernicke's hemianopic pupillary reaction, impairment of visual acuity in one or both eyes and gradual visual deterioration and bisection of the fixation point by the line of hemianopia.

The mechanism by which chiasmal injuries are brought about remains uncertain. The authors reject the view that a direct tear of the chiasm occurs and are of the opinion that the injury interrupts the vascular supply to the chiasm and so injures its conductivity. The chiasm is supplied by a rich network of vessels derived from the internal carotid arteries and their branches. These vessels at their origin are firmly fixed to the base of the skull, and any movement of the brain and chiasm relative to the skull may result in tearing these small vessels. In the same manner, tearing of pial vessels which supply the hypothalamus and the tuber cinereum readily explains the occasional occurrence of adiposity and polyuria in cases of chiasmal injury.

The authors noted similarity in the development of perimetric field changes in the three cases of trauma in their series and in cases of tumor pressing on the chiasm from below. This suggests that the mechanism of chiasmal injury is similar in tumor and in trauma. When the possible mechanisms by which the chiasm may be damaged in trauma and in tumor are considered, the obvious factor common to both is impairment of the vascular supply of the chiasm. In

trauma this is probably effected by violent rupture of some of the vessels, followed by surrounding local thrombosis and softening. In tumor a similar result is brought about by more gradual stretching and final obliteration of the vessels. It seems probable therefore that in both tumor and trauma interruption of conduction in the chiasm is dependent mainly on a gradual or abrupt impairment of its blood supply.

SALL, Philadelphia.

THE SENSATION OF VIBRATION, WITH SPECIAL REFERENCE TO ITS CLINICAL SIGNIFICANCE. I. GORDON, J. Neurol. & Psychopath. **17**:107 (Oct.) 1936.

In testing the sensation of vibration, the ideal method would be one in which: (*a*) the threshold is approached from below, (*b*) the result is given in millimeters of amplitude of the tuning fork, (*c*) the fork is not so cumbersome that it cannot be used in examinations as a routine and (*d*) the factor of fatigue is eliminated. Gordon has devised a quantitative method which fulfils these requirements and which he designates as the minimum threshold method. The Symns fork is struck and a stop watch started, at a known amplitude. About thirty seconds elapse before the fork is applied and the patient is asked if he feels the vibrations. If he does, the procedure is repeated, the fork being withheld for increasing periods until a time is reached when the vibrations cannot be felt. This is the threshold value for that bone. The amplitude decreases at a rate which can be plotted against the time. The points tested are the radius, ulna, sternum, sacrum, anterior superior spine, tibia and internal and external malleoli.

Normally, acuity of perception is diminished by fatigue, both extrinsic (fatigue of the organism as a whole) and intrinsic (overstimulation of the sensation of vibration). It shows variations on the two sides of the body, but neither side predominates. It may be increased by the training of sensation, both general and specific as in the blind. There is gradual loss of the sensation of vibration with increasing age, the loss being more marked in the legs, probably owing to arterial degeneration of the spinal vessels.

Gordon has applied his method in various disorders of the nervous system and has plotted his results against normal charts. In postencephalitic parkinsonism the curves were low, but within normal limits. Tabetic patients showed a "typical" curve with the loss of sensation in the sacrum ("sacral dip"). In syphilitic aortitis the diminution of sensation could be accounted for by the advanced age of the patients; in two cases there was absence of sensation over the sacrum, with involvement of the central nervous system in only one of these. In four of five cases of disseminated sclerosis there was marked diminution of vibratory acuity, this often being the only demonstrable sensory disturbance. In diabetes and pernicious anemia the method was valuable in detecting frequently involvement of the nervous system which would not otherwise have been disclosed. Although the absence of sensation over the sacrum is suggestive, Gordon does not believe that it is a sign of a pathognomonic lesion of the spinal cord. In general, testing of the sensation of vibration is most valuable in differentiation of pure motor and combined motor and sensory disease of the nervous system. It is the most delicate test of the integrity of the posterior columns of the cord. The sensation is perceived in the cerebrum—a protopathic element in the thalamus and an epicritic in the cortex. Gordon believes that most of the sensation of vibration is perceived by the deep tissues, to which the bone transmits its vibrations, and that only a small component of the sensation is perceived by the skin.

N. MALAMUD, Ann Arbor, Mich.

NOISES IN THE EAR, TINNITUS AND ELEMENTARY, COMMON AND VERBAL AUDITORY HALLUCINATIONS. FERDINAND MOREL, Encéphale **31**:81, 1936.

In classifying the heterogeneous phenomena of auditory disturbances, Morel follows the cochlear path as a guide. Peripheral noises of extraneural origin—muscular and vascular bruits—are characterized by monotony and relatively low complexity. The noises which originate in the cochlea, the primary neuron or

the projection fibers from the medullary nuclei to the cortex have the same characters. They are elementary noises and have no significance and no verbal form. They are localized subjectively near the ear, in the ear or in the head, but not in the sonorous space. Only the associated signs and symptoms can indicate the level of the lesion. An altogether different group of auditory phenomena consists of noises which are localized externally, in the subject's sonorous space. They are defined not, as in the preceding group, by onomatopœa but by direct reference to their supposed external source. The localization follows the laws of acoustics. These noises "irrupt" into consciousness in company with nonauditory elements, particularly tactile and visual, whence the cohesion of the entire process and the absolute, or almost absolute, belief in their reality. No gross cerebral lesion produces these phenomena. The functions involved are those which disappear in auditory agnosia. Just as auditory agnosia is generally associated with word deafness to some degree, these common auditory hallucinations are usually related to verbal hallucinations.

Verbal auditory hallucinations involve the phasic, or language, function. They depend on the patient's verbal ideation and are closely related to his character, prepsychotic habits and intentions. The voice is heard at any site, either in the patient's body or at any distance within or without the range of the normal voice. Its vocal characters are difficult to describe. The patient never imitates the voice. A general law, to which Morel has never seen an exception, is that two voices with different contents, or simply two systems of different phenomena, are mutually exclusive. They never occur at the same time, though they may alternate. It is best to observe these phenomena at the moment when they occur. In addition to introspection, objective methods should be used. They include observation of the patient's motor responses, particularly by the use of special recording technics, such as cinematography of the pupil, and sensory examination. Claude, Aubry and Baruk noted the inconstancy of labyrinthine reactions in paranoid dementia. Morel observed patients with chronic hallucinatory psychosis with the electric audiometer. A sudden, brief hypo-excitability almost always corresponded to an auditory verbal hallucination. Sudden disturbances in respiratory rhythm were noted by Paterson. Morel suggests the use of stroboscopic laryngoscopy and electromyography of the muscles of respiration, articulation or phonation. The importance of motor phenomena is shown by the attempts made by some patients to eliminate auditory hallucinations by inhibiting lingual and respiratory movements. One patient, accustomed to using a digital sign language, accomplished this by flexing her fingers strongly and asked that her fingers be cut off. The movements of phonation, however, are not sufficient. A special state, summarized as automatism, must be added to create verbal hallucination.

Tinnitus ordinarily has no relation to hallucination; yet in two patients with traumatic rupture of the tympanic membrane tinnitus was transformed into common auditory hallucinations attributed to an external cause when ether was administered or the patient was falling asleep.

LIBER, New York.

THE ARGYLL ROBERTSON SIGN. H. SCHAEFFER and MÉRIGOT DE TREIGNY, Rev. d'oto-neuro-opht. **14**:609 (Nov.) 1936.

Argyll Robertson described as the sign bearing his name abolition of the photomotor reflex, preservation of the pupillary movements of accommodation and corneal sensibility and only moderate dilatation of the pupil after instillation of a strong solution of atropine. Babinski required that the condition should be permanent, that it should be the expression of a lesion limited to the apparatus of the pupillary reflex and not allied to alteration of the globe or optic nerve and that it should not be associated with paralysis of the oculomotor nerves. Myosis is usual but is not always present. Pupillary immobility must be invariable, whatever the intensity of lighting or the duration of obscuration.

Schaeffer and de Treigny report thirty-three cases of undoubted syphilis of the nervous system in which all the pupillary reactions were investigated carefully and the condition of the irises was studied by means of the slit lamp and the

corneal microscope. Absolute or partial loss of the photomotor reflex (unilateral or bilateral) was present in thirty-two cases; in one the photomotor reflex was normal, but there was myosis with irregular pupils, poor reaction to the collyrium test and atrophy of the iris. In two of the thirty-three cases there was also loss of accommodation of convergence in one pupil.

Myosis was observed in ten of the thirty-three cases, in one of which the photomotor reflex was not lost. The opinion is expressed that in the remaining twenty-three cases one was not justified in assuming that the Argyll Robertson sign was absent. In the majority of the cases the collyrium test did not give normal results.

According to the criteria of Adie and of Merritt and Moore, the true Argyll Robertson sign is relatively rare in syphilis. This opinion is inadmissible. Myosis should not be considered an indispensable element in the sign. Although not in exact correspondence to the description of Argyll Robertson, dissociation of the pupillary reflexes, represented by loss of the photomotor reflex with conservation of accommodation of convergence, will probably remain a synonym of the Argyll Robertson sign. When the term is employed, it is important to specify what is meant. The conception of Babinski is irrefutable. In all cases the Argyll Robertson sign associated with lesion of the optic globe, optic nerve or oculomotor nerve must be regarded as suspicious. Dupuy-Dutemps called attention to the frequency of irregularity of the pupil and the importance of atrophy of the iris in cases of neurosyphilis. His dicta (1) that pupillary irregularity without apparent atrophy of the iris may be present and (2) that atrophy of the iris is always consecutive to the loss of the photomotor reflex, while true in the great majority of cases, do not constitute an absolute rule. The conception of Dupuy-Dutemps that the Argyll Robertson sign, the pupillary irregularity and the lesions of the iris which so often accompany it arise from a peripheral lesion involving the neuromuscular apparatus of the iris and the ciliary ganglion and nerves is discussed at length. Schaeffer and de Treigny are inclined to assume a double anatomic localization to explain these phenomena: (1) a lesion located in the peduncular tegmentum and involving the pupillomotor pathways and the sympathetic pathway and (2) a peripheral lesion, seated probably at the level of the ciliary neuron, causing atrophy of the iris. This hypothesis agrees best with the clinical facts.

DENNIS, San Diego, Calif.

BILATERAL REPRESENTATION IN THE MACULA. LEO KRAINER and KEISABURO SUWA, Jahrb. f. Psychiat. u. Neurol. **53**:35, 1936.

Krainer and Suwa report the case of a woman who, after extirpation of a tumor in the right occipital lobe, suffered bilateral secondary atrophy of the optic nerve and loss of vision, except light perception. She lived thirty-one years after the operation and died of poisoning from an overdose of barbital, which she took to relieve headache.

Histologic examination of the right hemisphere disclosed almost complete destruction of the caudal and adjoining part of the middle third of the area striata, with retrograde and secondary degeneration of the stratum sagittale externum, involving the oral as well as the caudal part of the middle layer of the visual medullary lamella. There was also almost complete degeneration of the middle portion of the caput of the external geniculate body and of the middle part of Wernicke's field; the oral third of the external geniculate body and of the field of Wernicke was well preserved. The oral third of the area striata and an adjoining portion of its middle third were unaffected and were connected dorsally as well as ventrally with the optic radiation. The dorsal and ventromesial portions of the stratum sagittale externum and the dorsomesial as well as the ventrolateral portion of the external geniculate body and of Wernicke's field were atrophied, but preserved. In the left hemisphere the optic radiation, the visual cortex and Wernicke's field were normal. There was neither circumscribed nor diffuse paleness of the left external geniculate body.

Krainer and Suwa conclude that, as the dorsomesial portion of the external geniculate body is connected with the dorsal layer and the ventromesial portion with the ventral layer of the stratum sagittale externum, the fibers from the middle portion of the caput of the external geniculate body must lie in the middle layer of the visual medullary lamella. As the mesial portion of the external geniculate body represents the projection area of the macula, macular fibers must form a bundle in the middle layer of the optic radiation.

The results of these investigations are contradictory to those of Rönne, Brouwer and Zeeman, which have been generally accepted as indicating the presence of a bundle of macular fibers in the dorsal portion of the optic radiation. As the fibers of Pfeiffer's bundle run not in the corpus callosum but ventrally and dorsally from the optic radiation into the homolateral area striata, this bundle cannot be accepted as subserving bilateral macular representation in the sense of Pfeiffer and Lenz. If there exists bilateral macular representation in the sense of Pfeiffer and Lenz, one would expect in cases of unilateral involvement of the visual tract and visual cortex, especially in lesions involving the macular region, changes in the contralateral external geniculate body. In the case reported in this paper, the authors were unable to see such changes.

KESCHNER, New York.

Encephalography, Ventriculography and Roentgenography

ROENTGENOGRAPHIC DIAGNOSIS OF RETINOBLASTOMA. RAYMOND L. PFEIFFER, Arch. Ophth. **15**:811 (May) 1936.

The clinical recognition of retinoblastoma is so difficult that error occurs in nearly one third of all cases in which the eye is removed for this disease. Therefore, any laboratory aid which distinguishes true tumor from pseudotumor is of interest.

Pfeiffer bases his studies on the fact that it has long been known that calcareous changes or deposits occur in retinoblastoma. He first studied twenty enucleated eyes with proved retinoblastoma and found that fifteen of the twenty specimens contained calcium deposits. In eight of a series of fourteen cases of suspected retinoblastoma, roentgenographic studies before operation confirmed the diagnosis. These tumors were later verified histologically. In four cases there was bilateral retinoblastoma, and in three shadows were seen in both orbits. In two cases calcium was not shown in the orbit before enucleation, and on subsequent roentgen and histologic examination calcium was observed to be lacking. In four cases pseudoglioma was observed on histologic examination, and in none was calcium shown in the orbits on roentgen examination before enucleation. In one case of pseudoglioma, however, a very small plaque of calcium was observed histologically in the organized tissue.

The calcareous degenerations are seen on the film as characteristic mottled or corneal shadows.

SPAETH, Philadelphia.

ENCEPHALOGRAPHY WITH ETHYLENE. HENRY NEWMAN, J. A. M. A. **108**:461 (Feb. 6) 1937.

Newman finds that the unpleasantness of encephalography is lessened and its scope of usefulness increased by using ethylene, which is only one-fifth as soluble as nitrogen monoxide, although still seven times as soluble as air. To date he has performed encephalography with the use of ethylene in 30 cases. In 24 of these visualization of the ventricles and subarachnoid channels was excellent; in 5, only fair, and in 1, poor. In this case, however, a subsequent trial with air yielded no better results. A survey of 189 cases in which encephalography was performed with air showed no higher percentage of satisfactory results. Because of the fairly prompt disappearance of ethylene in the subarachnoid spaces, it is essential that roentgen examination be made immediately after the injection, as a delay of as little as fifteen minutes may result in poor visualization. The headache complained of during injection of the gas did not differ in kind or degree

from that experienced by patients in whom air was injected. After the injection, however, the condition of the patient presented a striking contrast to that seen after the use of air. Most of the patients were comfortable within three or four hours and able to eat the evening meal, and in almost every instance they were up and about the following day. The average period of hospitalization following the procedure was reduced from three days, when air was used, to one and eighty-five hundredths days, with ethylene, while the condition of the patients on dismissal was in general better than after the longer period when air was used. That the shorter period of recovery from headache is due to more rapid absorption of ethylene seems probable. The author believes that the solubility of the gas, and not its anesthetic properties, is responsible for its advantage over air.

EDITOR'S ABSTRACT.

IODOVENTRICULOGRAPHIC PICTURE OF CHIASMATIC ARACHNOIDITIS. RAMON CARRILLO, Arch. argent. de neurol. **15**:74 (Sept.-Oct.) 1936.

Carrillo describes a ventriculographic sign which permits the certain diagnosis of arachnoiditis in general and of chiasmatic arachnoiditis in particular and of other conditions which may give secondary reactions of arachnoiditis. The iodoventriculographic sign of chiasmatic arachnoiditis consists of total or partial disappearance or deformation or fractionated filling of the infundibulum.

ALPERS, Philadelphia.

INTERNAL FRONTAL HYPEROSTOSIS: REPORT OF FOUR NEW CASES. T. FRACASSI and F. L. MARELLI, Rev. argent. de neurol. y psychiat. **2**:65 (April-June) 1936.

Fracassi and Marelli report in detail four cases of internal frontal hyperostosis, three of which occurred in women and one in a man. The majority of cases occur in women at the menopause. Headache and obesity are the most constant symptoms. The mental changes are varied, ranging from simple apathy or irritability to disorientation and delusions. At times various neurologic symptoms are present. Roentgenography discloses hyperostosis involving the internal face of the ascending part of the frontal bone, almost always bilaterally. There is no adequate explanation for the selectivity of this special form of hyperostosis.

It is difficult to make a clinical diagnosis of this curious syndrome without the roentgenographic findings. Headache, adiposity, symptoms of infundibulotuberohypophysial involvement, visual changes and evidences of compression of the frontal lobe are clinically of great value. Hypercalcemia when present is also a useful aid in the diagnosis. A diet low in calcium should be given. In some cases solution of parathyroid is indicated. If there is evidence of intracranial hypertension, operation must be performed.

ALPERS, Philadelphia.

VALUE OF INDIRECT ROENTGENOLOGIC SIGNS IN THE DIAGNOSIS OF TUMOR OF THE BRAIN. H. HELLNER, Beitr. z. klin. Chir. **164**:573 (Dec. 23) 1936.

Diagnosis of tumor of the brain must answer three questions: the location, the size and the nature of the tumor. According to Hellner, the usual roentgenogram of the skull is capable of contributing important information to these queries. Knowledge of the alterations caused by a tumor and visualized in an ordinary roentgenogram of the skull, while not as important as the neurologic examination and the knowledge of the course of an individual tumor, is nevertheless of considerable value. The author cites Kornblum, who observed in 446 cases of tumor of the brain in which the diagnosis was confirmed by operation or at necropsy that calcification was shown in 6.5 per cent. The types of intracranial tumor exhibiting bone formation were, in the author's experience, principally parasagittal meningioma, neurinoma and cholesteatoma. Here the roentgenogram furnishes information as to the localization, the size and, to some extent, the nature of the tumor. The author describes localized hyperostoses of the vault and the base of

the skull. These were likewise observed principally in meningioma, and occasionally in benign glioma and acoustic neurinoma. The roentgenogram furnishes information as to both the localization and the nature of the tumor in the case of meningioma. Histologic studies of meningioma characterized by a tendency to hyperostosis demonstrated invasion of bone by tumor cells. The roentgenologic and clinical differentiation of osteoma and meningioma no longer offers serious difficulty. One must be careful in interpreting erosions and atrophies of the skull. They can be caused by general increased pressure in the brain, as well as by the direct pressure of a tumor. They do not furnish any definite evidence of a topographic, qualitative or quantitative kind. The value of roentgenologic signs in the diagnosis of the nature of a tumor of the cerebellopontile angle is limited. On the other hand, the topographic diagnosis of tumor of the acoustic nerve is, as a rule, reliable. The side of the tumor cannot be told from a roentgenogram.

EDITORS ABSTRACT. [J. A. M. A.]

CRANIOGRAMS. Y. TAMURA, Psychiat. et neurol. jap. **39**:22 (Nov.) 1935.

Tamura reports the findings in 128 normal craniograms, 110 of which were taken in subjects over 15 years of age and 18 in subjects under 15. He finds that: (1) the coronal and lambdoid sutures were clearer and more constant in the younger age group; (2) the pineal gland was calcified in 13 per cent of adults; (3) the digital impressions were more marked in the younger age groups and in females; (4) the dimensions of the sella turcica were 12.9 by 11 by 9.8 mm.; (5) the circumference of the head paralleled the size of the sella; (6) persons of large stature showed a larger longitudinal measurement and a smaller depth of the sella than persons of small stature, and (7) persons of athletic habitus had normally a larger sella than others.

In fifteen cases of hypophysial tumor the findings were of the classic type. In thirty-two cases of trauma to the head Tamura found, in addition to fracture lines, other features, such as increase in the anteroposterior diameter of the sella and increased visibility of markings of vessels. In nine cases of narcolepsy the measurements of the sella turcica were normal. In thirty-five cases of schizophrenia studies of the skull revealed normal structure.

ALPERS, Philadelphia.

THE ENCEPHALOGRAM IN EPILEPSY. T. KANAHARA and Y. TAMURA, Psychiat. et neurol. jap. **40**:35 (July) 1936.

Encephalograms were made in twenty cases of idiopathic and in thirty cases of symptomatic epilepsy. In fourteen cases there was definite and in eleven slight dilatation of the ventricles. In three instances the ventricles were small. In eight cases there were no changes. In twenty-one cases there was marked difference in the size of the two lateral ventricles, and in six the third ventricle was dilated. The subarachnoid space was abnormal in fifteen cases. The longer the duration of the disease the greater the tendency to abnormal encephalograms. In only four of the twenty cases of idiopathic epilepsy were there normal encephalograms.

ALPERS, Philadelphia.

Society Transactions

PHILADELPHIA PSYCHIATRIC SOCIETY

Regular Meeting, April 9, 1937

FREDERICK H. ALLEN, M.D., *President, in the Chair*

A NEW METHOD OF TREATMENT FOR ACUTE POSTOPERATIVE AND POSTTRAUMATIC PSYCHOSES. DR. TEMPLE FAY.

The following case is described, as a matter of record, because it represents the first in a series of 7 cases of acute postoperative or posttraumatic psychoses in which treatment was directed along lines designed to quiet the patient through favorably altering the intracranial volume relationship and equilibrium by physiologic and hydrodynamic measures.

REPORT OF CASE

The diagnosis was tumor of the spinal cord and acute postoperative psychosis with recovery.

Mrs. L. C. was admitted to my service in the Temple University Hospital on Oct. 12, 1936, and was discharged on December 27. Three years before she had noted numbness in the left foot, followed by burning in the left foot and left leg, and subsequently numbness in the right leg. The tonsils and teeth were removed, but the symptoms progressed. About one and a half years later numbness and pain had extended to the abdomen and became intense in the left shoulder and left arm. There had been inability to walk for two years.

Neurologic Examination.—On October 13 there was marked impairment of touch, pain and temperature sensibility below the third thoracic dermatome bilaterally. This included the axilla and a line anteriorly about 3 inches (7 cm.) above the level of the nipple. There was loss of position and vibratory sense below the waist. There were patellar clonus on the right and ankle clonus bilaterally. A Babinski sign was present bilaterally. There was exaggeration of tendon reflexes in both lower extremities. Pain and temperature sensibility was more involved on the right than on the left.

Roentgenologic Studies.—A spinal roentgenogram was normal. Injection of air revealed disturbance to passage of air at the third thoracic lamina, with complete block. The Queckenstedt test showed complete block.

Operation.—On October 23 I performed an exploratory laminectomy with local anesthesia fortified with 3.7 cc. of avertin (tribromethanol in amylene hydrate). An encapsulated tumor, about the size of an almond, was observed beneath the dura, at the left side of the cord under the third thoracic lamina. It arose from the third thoracic root and had compressed the cord to the right. It was completely removed. The operation lasted three hours and five minutes. The patient was returned to the ward in good condition, the blood pressure being 134 systolic and 80 diastolic, the respiratory rate 24 and the pulse rate 112.

Pathologic Diagnosis.—The tumor was a schwannoma.

Course.—Postoperative recovery was good; no transfusion was required, owing to the minimum loss of blood at operation, and there was no shock. The patient was comfortable. Soluble phenobarbital U. S. P. (sodium phenobarbital, N. N. R.) 1½ grains (97.2 mg.), was given at 8 and 11:30 p. m.

The patient's condition was good on the following morning; she was cooperative and complained of pain in the area of operation. She was restless in the evening, becoming excited and requiring ½ grain (32.4 mg.) of codeine sulfate and ⅙ grain

(10.8 mg.) of morphine sulfate every four hours, with temporary relief from restlessness. The temperature was 98.3 F., the blood pressure 108 systolic and 74 diastolic, the pulse rate 100 and the respiratory rate 20. Ten grains (0.648 Gm.) of sodium bromide and 5 grains (0.324 Gm.) of chloral hydrate were given every three hours, but marked restlessness with sweating and resistance to restraint continued. Again, ⅙ grain of morphine with 1 grain (64.8 mg.) of codeine sulfate and 1 grain of phenobarbital produced a short interval of rest.

On October 25 the patient was markedly psychotic, with incoherence, shouting, screaming and blubbering; she did not recognize the family and did not respond to suggestion or command. She was negativistic and restless and was kept in restraint. She refused food, made incoherent sounds and was apprehensive. These symptoms subsided with periods of exhaustion. The upper layers of the wound were pulled open by constant muscular strain. Thirty-two ounces (946 cc.) of fluid was given by rectum.

On October 26 the fluid was increased to 60 ounces (1,774 cc.). The patient's condition remained unchanged. Laboratory studies revealed: blood urea, 40 mg. per hundred cubic centimeters; blood sugar, 143 mg.; red blood cells, 4,020,000, and leukocytes, 14,000. The rectal temperature was 102.6 F. The pulse rate was 130. On the following day the condition was much the same.

The diagnosis was acute postoperative psychosis.

After staff consultation, it was decided to attempt to produce a "wet brain" and stupor in order to quiet the restlessness and constant noisy manifestations.

Spinal puncture was performed, and 60 cc. of sterile physiologic solution of sodium chloride was rapidly injected into the spinal canal in order to raise the pressure sufficiently to "knock the patient out"; 750 cc. of physiologic solution of sodium chloride was also given intravenously. Fluids (120 ounces [3,760 cc.]) were given by mouth, and 20 cc of a 20 per cent solution of sodium chloride was injected intravenously.

After the intraspinal injection and intravenous and oral forcing of fluids, the patient became quiet and began to improve within three hours. On the following morning she was rational, cooperative and coherent, with no recollection of the preceding period of psychosis. Speech was normal, and the anxiety and apprehension were gone. The intake of liquids was 92 ounces (2,720 cc.), and the output, 46 ounces (1,360 cc.). The rectal temperature was normal; the pulse rate was 80 and the respiratory rate 22. There was also recovery of continence. The patient was removed from restraint, and sedatives were discontinued. Convalescence followed a normal course.

Summary and Comment.—From October 29 to the present the patient has been clear, coherent and cooperative. Local infection of the wound, due to contamination during the postoperative psychosis, has required continual dressing for a superficial sinus. Leukocyte counts ranged from 9,000 to 14,000 during the psychotic episode. The urea content of the blood on October 31 was 15 mg. per hundred cubic centimeters.

The patient made a gradual and uneventful recovery, with return of function in the lower extremities, sensory improvement and beginning ability to walk on November 7. On November 26 she walked unassisted, and her condition was normal except for the wound, which continued to drain and was dressed daily.

The patient was discharged from the hospital on December 27, with almost complete return of sensory and motor function in the lower extremities.

A case of acute postoperative psychosis extending over four days is described. The usual measures of sedation and medication failed to quiet the patient. A deliberate attempt was made on October 28 to produce cerebral edema and unconsciousness. Experience in handling problems of cerebral edema and stupor by means of "dehydration" offered an opportunity to treat the opposite condition (manifested by a psychosis with increased mental activity), which failed to respond to routine or heroic administration of sedatives. By completely reversing the routine of "dehydration," an acute state of hydration was produced.

In an attempt to produce acute cerebral edema by overloading the brain and cranial cavity with fluids (hydration method of Rowntree), the patient was rapidly brought back to a normal mental state, and the anticipated production of stupor or unconsciousness did not appear. The patient awoke instead to a state of full comprehension and cooperation.

The patient's manifestations were not those of uremia. She received after operation the amount of fluid usually adequate in such procedures on the spinal cord, and, being fat and overweight, was not "dehydrated" at any time. In my opinion, the following explanation is reasonable.

The patient lost spinal fluid during the period in which the canal was open and the tumor was being removed. Fluid was also lost through the skin by profuse sweating following operation. Hardly 2 ounces (59 cc.) of blood was lost during the laminectomy. The chloride content of the blood was 504 mg. per hundred cubic centimeters on October 27 (normal content, from 430 to 520 mg.). During operation the head was maintained in a slightly dependent position, favoring hyperemia and overcongestion of the cerebral vasculature. The loss of spinal fluid from the cranial cavity allowed excessive blood to accumulate in volume equal to that of the spinal fluid lost (Monro-Kelly doctrine).

Direct introduction of sterile solution of sodium chloride into the spinal canal in large quantities (from 30 to 60 cc.), sufficient to push from the craniovertebral cavity an equivalent volume of circulating blood and to raise the intracranial pressure temporarily to at least 20 mm. of mercury, had a physiologically quieting effect on the patient's restlessness and excessive mental activity, with return to a more normal mental state.

Introduction of a sterile physiologic or hypotonic solution of sodium chloride by vein promotes and enhances storage of fluids in the tissues, with increase in the production of spinal fluid (Weed). As the volume of spinal and tissue fluid within the cranial cavity increases, there follows a reciprocal decrease in the volume of circulating blood, because the cavity is incapable of expansion. The result is that with excessive volume of fluid one may approach a state of cerebral anoxemia due to reciprocal loss of circulating blood and oxygen.

Between extremes of stupor (anoxemia), on the one hand, and excessive mental activity (hyperoxemia), on the other, lies a zone of "normal," in which the person finds at times a desirable state of "dulness" and mental retardation when the volume or pressure of the fluid is increased. This may be normal in sleep or drowsiness following excessive indulgence in fluids or food. Pathologic processes, associated with disturbance in accumulation or elimination of cerebrospinal fluid, are notorious for their depressing effect on psychomotor activity.

When mental acuity and alertness are required, improvement may be obtained in cerebral circulation by increasing the speed of flow of the blood (by vasoconstrictor drugs), raising the blood pressure or increasing the volume of blood circulating within the cranial cavity. Increase in the volume of blood requires reciprocal diminution in the volume of the fluid component. Thus, during periods of physiologic subtraction of spinal fluid from the cavity under normal conditions (exercise with sweating, purgation and general measures of "elimination") hyperemia ensues, or, in the thin, underweight person with excessive dynamic psychomotor activity, the process may become pathologic. When dehydration and emaciation occur, the loss of tissue fluids favors cerebral hyperemia.

Is it possible to visualize a spectrum of mental activity, ranging from stupor, on the one hand, to hyperexcitability, on the other, with a correlating curve that concerns primarily the volume of oxygen available for metabolic processes through the circulatory mechanism?

This embraces the entire physiology of oxygen in its ultimate delivery to the cell, and there are innumerable physiologic interrelationships with local and distant pathologic processes that may influence in varying degrees the actual availability of oxygen to the cell.

In this paper I have called attention to a factor relating to the volume of blood within the cranial cavity which may directly or indirectly influence favorably the normal equilibrium and balance between circulation and cellular activity.

Conclusion.—This preliminary report justifies no definite conclusion. There is, however, a strong indication, based on present knowledge of altered fluid relationships within the cranial cavity in known conditions of excessive fluid processes associated with mental dulness and stupor, to justify the assumption that the reverse of this condition might be associated with hyperfunction and activity. Knowledge in this field, however, is limited at present, and further studies along the lines of intracranial volume relationships rather than of pressure are indicated.

DISCUSSION

DR. ALFRED GORDON: It may be of interest to Dr. Fay to know that for several years I have been treating patients with serous meningitis accompanied by mental symptoms in this manner. In the 2 most recent cases meningitis with delirium, confusion and restlessness was presented. Ordinary remedies were tried without effect. I then withdrew spinal fluid and injected into the spinal canal twice the quantity of a solution of sodium chloride. In two days the patients began to recover. I wish to ask Dr. Fay whether in his case the injection was preceded by withdrawal of spinal fluid? I wish not to take priority from Dr. Fay but to mention my long-standing observations, which are somewhat similar to his.

DR. TEMPLE FAY: In my experience 60 cc. of sterile solution of sodium chloride is sufficient to bring about the desired result, if a pressure of 20 mm. of mercury can be maintained.

In 2 cases a definite reaction followed with headache and manifestations similar to those of mild meningitis. These symptoms disappeared a few hours after injection.

It is important that the temperature of the solution should be maintained at about 100 F.

BEHAVIOR, PERSONALITY AND INTELLIGENCE OF CHILDREN WITH ENDOCRINE DISTURBANCES. DR. MATTHEW MOLITCH, Jamesburg, N. J.

About 25 per cent of the population of the New Jersey State Home for Boys have some degree of endocrine dysfunction. The inmates range in age from 8 to 17 and have all been committed by court for overt behavior. Over 50 per cent of this group have pituitary dysfunction, while only 6 per cent have a thyroid disorder. The rest have gonadal disturbances, ranging from delayed secondary sexual development to hypergonadism. The intelligence of the boys with hypopituitarism and hypogonadism is more often subnormal than that of the group used as a control. The groups with hypothyroidism and hypergonadism show more cases of subnormal, but also of average normal, intelligence than the control group. Certainly, all children with endocrine disorders are not feebleminded.

Children with endocrine disorders are, as a group, more unstable and do far worse school work than the control group. Sensitiveness about their physical differences is more marked in some children than in others, but I have not found it to be a serious problem. Children with gonadal disturbances are the most seriously unstable, especially those with undescended testes. Their school work is much below their ability, and truancy is present to a considerable degree. Several of the children with hypergonadism are sexually preoccupied and present homosexual problems. The high incidence of endocrine dysfunctions in persons with behavior problems should stimulate more research on the probable causal relationships.

DISCUSSION

DR. L. H. SMITH: Dr. Molitch's important presentation contains much more material than at first meets the eye. There has been little observational and scientific work done in institutions of the type from which his material has been gathered. Controlled studies of this sort bring to light some significant facts. As children with endocrine disturbances pass through the various stages of childhood,

it has been observed that the physical, mental and endocrine changes are not exactly parallel. Dr. Molitch has pointed out extremely significant curves for hormonal and gonadal changes which indicate that these processes may be retarded in one child and stimulated in another. If the same series of children can be studied in terms of hormones by laboratory examination, parallel findings may be established. In these children significant emotional aspects were connected with the height, size, strength and ability; my colleagues and I are particularly conscious of the extreme sensensitiveness of some boys about their secondary sex manifestations. As a result, actual emotional aspects may have an effect on the behavior in general. I think Dr. Molitch's paper will bear a great deal of elaboration and, together with hormonal studies, will give something conclusive, which is clinically applicable and useful.

DR. MATTHEW MOLITCH: In answer to Dr. Smith, I wish to state that the emotional reactions of these children are on an individual basis. It is surprising to see how much different a boy can be from the rest of the group and still not feel sensitive or out of place. More depends on the individual personality and psychic make-up. In the majority of cases, children with the Fröhlich syndrome correct themselves without treatment. My associates and I treat them only if they fail to show improvement by puberty or if they are too obese. I considered biologic assays for estrogen and androgen and for the growth hormone but was advised against it because of the expense and unreliability of the present methods.

DEVELOPMENT OF LANGUAGE FUNCTION IN CHILDREN. DR. PAUL C. DOZIER, New York.

For clinical study, the language function may be divided into four fractions: understanding of the spoken word, speech (defined as the spoken word only), reading and written expression. The various types of aphasia and agraphia provide examples of partial or almost total destruction of one or more of these fractions, the defect in these cases being most conveniently described as one of association. Similar imperfect language associations exist in some persons as a constitutional defect and not as the result of a progressive pathologic process. These congenital or developmental "aphasias" do not have their origin in the emotional field, as may speech disturbances of another class in which the language function is disused but potentially intact. The developmental group includes: so-called word deafness, in which understanding of speech and speech are affected; motor delay, in which speech alone is affected; specific reading disability, and specific difficulty with spelling. This true disability in learning to read (strephosymbolia, or word blindness) is an appropriate example by which to indicate the group because of the numerical importance of the cases. Also, this form has been more extensively described than the others, and there is indication that it is a definite constitutional type which is subject to alteration. It must be distinguished from a larger and heterogeneous group in which some kind of trouble with reading is a complaint. Difficulties occurring with general mental retardation, visual deficiencies, emotional maladjustments and inadequate training all have features peculiar to themselves. Furthermore, if pure, they lack the essential feature of the specific group: persistent failure in the recognition and recall of written symbols, an error which is more prominent as the symbols are more complex or less familiar. In simple terms, children with this disturbance cannot remember what letters and words look like.

Since the presenting complaints are various and the histories of the children far from uniform, specific reading disability must be defined by psychometric and educational tests, special language tests and understanding of the personality, especially as it has attempted to adjust to its lack of success. As a result of such studies in a number of cases, these statements can be made regarding the group as a whole: (1) There is normal, often superior, intellectual ability where reading or reading experience is not concerned; (2) the understanding and speaking vocabularies are normal; (3) facts acquired by ear are well retained; (4) disability in spelling is almost always present; (5) there is no difficulty with mathematical reasoning or calculation in ordinary cases; (6) a partial, but inadequate, reading

and spelling vocabulary may have been mastered by rote through frequently repeated exposures to the same words; (7) in many cases there is a degree of confusion in discrimination of certain elements of the spoken language and in their reproduction, this being less marked than the confusion in visual language, which identifies the condition; (8) in some cases particular errors in speech and handwriting suggest confusions in the kinesthetic and motor fields; (9) an emotional adjustment problem is the rule, accompanying or resulting from the reading difficulty and failure in school; (10) of the patients exhibiting this difficulty the far greater number are boys; (11) that the defect is to some extent familial is suggested by the presence in other members of the family of special reading disability and other language disabilities.

In addition to these general features, Orton originally noted the occurrence of five sinistral factors in this group: reversals, mirror reading, mirror writing, left handedness and left eyedness. Although no one of these conditions is diagnostic in a case of specific reading disability, the persistent presence of any one or more of the first three is common; in a large series of cases, in which analysis is not yet complete, the incidence of all five factors is great. Although these observations have not been adduced as proof, they logically suggest divided function of the two cerebral hemispheres (or unevolved unilateral function) as an explanation of the difficulty.

Treatment consists in technical reeducational measures in language, planned for the individual child, readjustment of school and home programs and attitudes and such psychiatric guidance as is necessary. Although reeducational measures call for a certain technical knowledge of language structure on the part of the tutor, the principles are simple. Words must be reduced to their parts for study, and as these letters and larger units are mastered they are combined in progressively longer sequences. Simultaneous seeing and sounding and hearing and writing and other associations of language units and words are exercises which must be repeated from scores to hundreds of times, as often as is necessary. The various groups of language units which are unevolved, interchanged or otherwise confused must be given frank overemphasis to promote their distinction. Most important, there must be deliberate reenforcement of the three sensory components one by another, especially that of the comparatively inefficient printed symbol by its repeated use with the comparatively efficient spoken symbol. There must also be linkage of the corresponding motor to the sensory element of a language symbol by promoting immediate oral or written response to the visual or auditory stimulus. When such principles are meticulously applied to the many points of confusion where they are called for, and only to these points, they are successful in the average case in bringing about a gain in reading and spelling of more than one school year per year. Much of the material of other subjects in the school curriculum should be given to the child by word of mouth until reading is up to grade. Attempts to instruct by the sight method and by rote memorizing are avoided as wasteful. Special help always requires a number of months, and often a certain amount of technical guidance is required for years.

The group with this disability presents as many types of personality and environmental situations as may be gathered under the banner of a single biologic characteristic. The various emotional difficulties encountered are not always secondary to the native language defect and must be individually managed. Many children are inadequately treated because of neglect of technical help or of management of the total situation.

In summary: Specific reading disability may constitute a practical educational block—and hence a reason for seeking consultation—at any point in the school career. Children with mild degrees of the difficulty are usually passed from grade to grade until at last they emerge as school failures. The condition is manifest in children of all ranges of intelligence, from the very superior to those of borderline mentality, and has been demonstrated in the groups of high grade morons. It is specific to the degree that it falls below the various aspects of general intellectual ability, and may be mild, moderate or so severe as to merit the term "word

blindness." Any kind or degree of emotional problem may be associated with it. The ultimate reading ability is dependent on such factors as age, intelligence, degree of disability and efficiency of the remedial and adjustment program; in all cases, however, in which the intelligence is near the average range proper treatment brings about some ability to read, which may be advanced indefinitely.

DISCUSSION

DR. TEMPLE FAY: In my opinion, there is a definite relationship between the handedness of a person and certain difficulties in speech. I have observed several cases of latent left handedness in which reenforcement of the left hand or movements of the left leg facilitated speech in apparently right-handed patients with delay in starting sentences or mild stuttering. Definite tests should be made to determine whether speech is improved by movements of the left or right hand. A conflict may exist between areas for speech memory; the following example indicates at least separation between use of the spoken word in prose and association of the same words with music or song.

In a recent case in which there was a large endothelioma in the left temporoparietal region, over the angular gyrus, jargon aphasia developed, with progressive loss of the ability to speak. Motor function was not involved. Prior to operation, at which the tumor was removed, the patient was able to say a few words; for two days afterward no definite words were obtainable. As speech returned on the third day, he could make a few distinct pronouncements, but when asked to sing "My Country 'Tis of Thee," he rendered the full verse without hesitancy or disturbance in speech mechanism as long as the tune was carried with the words. If, however, he was asked to say the words without musical intonation or to repeat the words after the examiner, there was inability to make more than crude sounds, and the effort was given up with hardly a distinct word having been uttered.

This indicates definitely that the pathways for speech may vary, depending on the association of the word with music or its direct use in prose.

DR. PAUL C. DOZIER: Dr. Fay's remark regarding the relationship of latent left handedness to speech block is interesting. Various observers agree on the prominence of mixed or indeterminate factors of handedness in a certain proportion of speech disabilities. I cannot explain in terms of pathways the cause of the disturbance in cases of aphasia, such as the one which Dr. Fay described. There are analogies to such conditions in cases of congenital aphasia in very young children. I know especially of a child, 5 years of age, who could not speak but had musical ability and could memorize songs to hum. In infant development vocalization with changes in pitch is often prominent, to be replaced later by patterns of speech in which pitch is not much concerned. Also, cases of amusia associated with lesions of the cerebral hemispheres have been described in which there was loss in previously efficient musical skill, just as in aphasia there is loss of previously efficient language function.

DR. R. A. MATTHEWS: I wish to know how frequently Dr. Dozier has encountered children with a diagnosis of feeblemindedness who had only a language or a specific reading disability?

DR. PAUL DOZIER: The diagnosis of feeblemindedness is frequently made in case of the strephosymbolic person of normal intelligence. I know of a score or two of cases in which this label has been attached by a teacher or a psychologist, and sometimes by a physician.

PSYCHOTHERAPY IN CASES OF SUSPECTED ORGANIC DEFECTS IN YOUNG CHILDREN. DR. OSCAR PAUL HOLMER, Reading, Pa.

This report of a case concerns the treatment for two years of a girl aged 3½ who presented the chief problem of apparent deafness and failure to talk. The child's mother visited many specialists in various cities in the East. Many contradictory diagnoses were made; some regarded the child as deaf, and others, as

feebleminded. Naturally, these frequent contradictions upset the mother. She was unwilling to believe that the child was feebleminded and had considerable doubt about actual deafness. She noted that the child seemed to hear at certain times and failed to hear at others. Finally, the child was studied in a play situation in which the main emphasis was placed on unhurried observation and treatment, with no particular pressure to arrive at an immediate diagnosis. She was seen on the basis of one hour a week. It soon became obvious that the child had no defect in hearing; she presented a definite behavior disorder. She was extremely negativistic, violent and destructive and unable to tolerate limitations of any kind.

The psychiatrist's task became one of helping the child relate herself to the reality situation. In the first hours of treatment she had to be restrained from leaving the office. This resulted in violent assaults on the psychiatrist. Later, as she acquired a great deal of positive feeling for the psychiatrist, there developed a struggle over leaving and a good deal of jealousy of other children who came for treatment. It is interesting that the child's failure to respond to sound stimuli disappeared coincident with the working through of her extreme negativism in the early weeks of treatment. She began to talk at the same time.

The various mechanisms demonstrated by the child in the course of treatment and the therapeutic measures used are described in some detail. Therapy centered largely around the child's rejection of reality, the psychiatrist constantly representing the reality situation to her and gradually accomplishing its acceptance through the relationship with her. Certain well defined limitations were imposed. These came to represent the demands of reality during the treatment hour. At the same time, the psychiatrist tolerated and accepted the negative and hostile behavior and in this way lent support to the weak ego of the child.

It was clear in the second and third hours of treatment that deafness did not exist and that the child was able to talk. A great deal of needless anxiety had been stirred up in the mother through incorrect diagnosis. The use of play technic or the therapeutic situation as developed in child guidance clinics is an aid to diagnosis which should not be neglected. The use of this type of study might contribute a great deal toward accurate diagnosis in case of young children.

DISCUSSION

DR. F. H. ALLEN: I had one interview with this child, when the family brought her in for observation; at that time she presented a puzzling diagnostic problem. She had been seen by a number of otologists, many of whom had given the opinion that she was deaf. In the first contact with the child I was struck with the sweeping nature of her negativistic behavior. Her determination was such that she had to fight any kind of limit, and her behavior was of a blind and destructive type. I referred her to Dr. Holmer, with the suggestion that he observe her for a number of weeks to see what movement would follow. Treatment was started partly to see if therapy was possible and partly to use the contact to clear up the diagnosis.

Dr. Holmer's discussion of the material indicates the value of approaching the problem in this way, for it became increasingly clear in this case that the child did not have an organic difficulty in the ear but that the problem was entirely psychologic. The material that Dr. Holmer has presented in this paper is interesting, and I wish there were more time to discuss it. As I interpret some of the material, the child has been fighting against everything which involves growing up. Growing up for her would have meant accepting the fact that she is a girl and a person in her own right. She seems to be constantly fighting against this, especially against accepting the fact that she is different from the brother toward whom so much of her antagonism is directed.

It is important to see this case as a problem of growth and not to become too much involved in it as one of castration. If one were to describe it as castration anxiety one would see it as a sexual problem, whereas I believe it is primarily one of growth. The child seems determined to hang on to infancy, and a great

deal of this determination has been directed toward making herself just like her infant brother. It did not take long for her to focus a good deal of her turmoil in the therapeutic treatment, as she established her relationship with Dr. Holmer. That he was able to set limits and help the child to live within them made it possible for her to grow a little within this relation. The mother could not set these limits; therefore the child was in complete control of everything that happened at home. As she established the relation with Dr. Holmer, she made it total and sweeping. It was as if she was trying to own Dr. Holmer, and she attempted to do this through showing him much of her affection. Her affection then became her means of attempting to own him, just as her failure to speak and her apparent inability to hear were the ways in which she had gained complete control over the situation at home. When the child found she could accept some limits from Dr. Holmer, she was then in a position to grow a little on her own account.

One of the important problems in this case that Dr. Holmer will have to meet from this point is that of helping the child to leave, so that in ending this treatment there will be some of the most effective therapeutic work. The tendency will be for the child to hang on to treatment and to do so by clinging to some of her behavior difficulty.

DR. O. S. ENGLISH: Since the time is short, I shall limit myself to one comment; that concerns the normality of the parents in a case of this kind. One is constantly seeing neuroses and psychoses in children from homes of so-called normal parents. One must have a more accurate method of deciding on normality, or else have it established that certain normal parents have attitudes which prevent normal emotional development and expression in children.

There has been an interesting change through therapy in a case in which a psychosis seems to have been developing at an early age.

DR. PAUL HOLMER: I have elaborated the frequent struggles in which the child engaged over leaving the office when the hour was up. The question whether she was suffering from castration anxiety or conflict over difference was not discussed. In response to Dr. English's question about the normality of the parents, I may say that this was recognized as only apparent. The mother was seen for a total of about twenty hours but never on a treatment basis—only as she showed concern about the child. Purely superficial observation suggests that she has anxiety only about the child.

Regular Meeting, May 7, 1937

FREDERICK H. ALLEN, M.D., *President, in the Chair*

THE SENSE OF GUILT AND THE NEED FOR PUNISHMENT. DR. MARGARET DE RONDE, Norristown, Pa. (by invitation).

Some of the underlying factors of human behavior are directly responsible to a sense of guilt. From the psychoanalytic standpoint, the sense of guilt has been widely investigated, and reference has been made to the relationship of a sense of guilt and need for punishment to criminality. Two cases are cited not only to show that a sense of guilt and need for punishment played a large part in the psychoses but to trace these factors through the patients' lives, thereby establishing the existence of certain patterns of personality which lead logically to the types of psychoses present.

UNCONSCIOUS HOMOSEXUALITY. DR. SAUL STEINBERG, Norristown, Pa. (by invitation).

In the course of normal psychosexual development heterosexual tendencies predominate, while those of a homosexual nature, although they do not disappear

entirely, are submerged and deflected in their aims. Owing to faulty psychosexual development, some persons form homosexual tendencies to such a degree that the entire personality is predominated. When this occurs, the adult genital level is not reached; fixations at pregenital levels result; if these trends are recognized, the person may solve his problems in overt homosexuality, and if not, in sublimated homosexual activities. Failure in sublimation may result in psychotic social behavior. Two cases are cited, with the thought of tracing unconscious homosexual trends.

ROLE OF THE WISH-FULFILLING MECHANISM IN PSYCHOSIS. DR. MOLLIE E. ORLOFF, Norristown, Pa. (by invitation).

It is shown that the psychotic person clearly presents the many unfulfilled dreams, desires and ambitions in his wish-fulfilling fantasies. Many are dissatisfied with some phase of their living. All dream or wish that things could be different than they are. This process begins in early childhood. In some the wishing or dreaming may occupy the whole conscious life. This is seen in the psychosis.

The wish-fulfilling fantasy was observed in 2 patients: a woman aged 68 and a man aged 26. In each case the wish-fulfilling fantasies were traced into a fully developed psychosis, which led to marked satisfaction in the patient's adjustment to life.

DISCUSSION ON PAPERS BY DRS. DE RONDE, STEINBERG AND ORLOFF

DR. O. SPURGEON ENGLISH: I am glad to hear so much dynamic psychology presented by the staff of a state hospital. Formerly, it was only the sporadic psychoanalyst who was supposedly flighty enough to utilize these concepts, applying them to neuroses and particularly to psychoses. These state hospital physicians have their feet on the ground and when they utilize freudian psychology in understanding their patients, it must mean something. Some who are willing to understand the psychosis in this way and are interested particularly in treatment may raise this question: Suppose one knows all about the guilt or the unconscious homosexuality in a given case, what can one do about it? In many cases it is very difficult to do anything when the guilt, for instance, has become too great. That, of course, is why psychologic treatment takes so long. When the guilt reaction has been developing for twenty years it has developed for a purpose; it serves as a protection against something, and it is difficult for the patient to part with this pattern of reaction. It takes a long time to "drain off" this quantity of emotion. However, in many cases it can be done, and sometimes, even in the psychosis, I believe that utilization of these psychologic concepts has definite values in mental hygiene, of which I may mention at least two: First, by applying these concepts to the psychosis and understanding of the patient, one is better able to give advice when the patient leaves the hospital, both to the patient and to his friends. One can anticipate problems that may arise and warn the patient of things he should avoid. Second, a more general value, and one looking farther into the future, is that when these principles become better known something can be done to prevent such tremendous accumulations of guilt or the development of too many wish-fulfilling fantasies. I believe that the time is coming when the terms "guilt" and "aggression" will mean something to the man on the street—just as it has come to be known that pain in the abdomen may mean something serious, like appendicitis, or that loss of weight and cough may mean something dangerous, such as tuberculosis. It will be understood that these quantities of guilt and aggression which are seen developing in young persons may lead to something serious, such as a psychosis or at least a severe neurosis. I have enjoyed these presentations.

DR. SAMUEL W. HAMILTON, White Plains, N. Y. (by invitation): I shall address myself to two points, one of which appears particularly in the cases that Dr. De Ronde described—the great practical difficulties that are produced by the persons who want to be punished. I have been observing for the last twelve years a series of persons from comfortable homes, some from more than com-

fortable homes—persons who have a cultural background, a good intellect and good education. It is a selected group in these respects, and, by the same token, the patients are well prepared to outwit those who care for them. In cases in which this desire for punishment exists, I assure you it has been a difficult thing to prevent the punishment from becoming vital. One cannot be too careful of these patients who are particularly keen about hurting themselves. A young man, for instance, when given the slightest opportunity, picked up the foot of his bed and dropped it on his toes. A successful business man in middle life was badly injured one day by another patient, who hit him in the face with a heavy lamp. It turned out that the second patient had plotted to hit this man and to be hit back with the lamp. The patient was not attempting to cause difficulty for others; he was just trying to cause trouble for himself. One cannot always convince the relatives about those who are trying to get others to hurt them.

Second, with regard to such women as Dr. Steinberg has discussed: From my experience in a state hospital that drew on a population of relatively comfortable, reasonably intelligent, people, one woman after another complained that in her early life, or maybe later, she had committed sexual improprieties, and for these she was blaming herself. In many instances what the patient said she did was so, and in some instances it was thought that it was not. At any rate, as has been pointed out, what comfort have these patients except in their delusions? There are times when it is cruelty to relieve the patient of his fantasies, but most persons should be relieved of them as far as possible, because there is likely to be a situation that may be stated thus: "Although I am perfectly happy in these ideas, the people surrounding me have taken me away from my home and are keeping me from the things that I want to do and are crushing this personality that has only lately been able to expand as I am now expanding it." The physician can often penetrate and modify the situation. Of course, many paranoid persons, if given time, will reach a point where they stop talking about their troubles. One man who was in a hospital eleven years and after that time went back to his old job, had, I am sure, no particular dynamic attack made on his difficulty. In many instances a dynamic attack helps the patient to get in reasonable rapport with the world sooner than he otherwise would.

DR. ARTHUR P. NOYES, Norristown, Pa.: There is an aspect which I think may not have been sufficiently stressed. It seems to me that the same psychologic themes which influence the psychosis are active in determining character traits long before the psychosis appears, going back, in fact, to early life. In most cases it will be found that the character traits which were peculiar to that person all through his life were determined by these psychologic themes. Dr. De Ronde described the case of a woman who was so scrupulous and meticulous, and I suppose was known as such a good housekeeper, that she was more or less a joke among her friends. It may well be that these character traits were determined by the same sense of guilt that has been a dynamic factor in determining her present mental disorder. I believe that in many instances personality traits are determined by psychologic themes some of which have been discussed tonight. In most persons the character traits which result through the dynamic action of these themes are sufficient to meet the specific personality and emotional needs. In other cases they form what is in effect the first line of defense, which, however, unfortunately may break down, in which case the psychosis is the next step to which resort is taken.

DR. JOSEPH C. YASKIN: For the benefit of the Norristown State Hospital staff, I wish to call attention to the fact that they have a patient who beautifully portrays "the sense of guilt and the need for punishment," "unconscious homosexuality" and the "wish-fulfilling fantasy." This patient had been under my care for a number of years; he was studied at the Pennsylvania Hospital, I think for three years, and was transferred to the Norristown State Hospital about two years ago. In his case there is really a combination of all three factors. I wish to add a point. I think that psychologic mechanisms are useful in understanding the psychosis. Some believe they do not explain the nature of the psychosis; in

other words, there is the feeling that beyond the psychologic mechanisms there is a definite organic situation. I speak now of the psychosis only, not of the psychoneuroses; I believe one must be cautious, especially in case of the young, not to get the idea that the wish-fulfilling fantasy, the feeling of guilt and the need for punishment explain everything in the psychosis. These are only superficial manifestations of a much deeper process; I think the latest addition to treatment, the insulin shock therapy for dementia praecox, is conclusive proof that psychology furnishes only part of the story of the total situation.

DR. FREDERICK H. ALLEN: I wish to make one or two comments on points that have been raised in these discussions. One must be careful in psychiatric work that when one thinks in terms of mental mechanisms one does not become too mechanistic in one's thinking. Dynamic concepts can become static, and in some aspects of psychiatry it seems as though that has happened. I believe that this is true in case of the concept of homosexuality as it was given in the first case. The concept of homosexuality that has been given tonight seems more mechanistic than dynamic, and I believe that there is need of revamping this theory and introducing into it more dynamic concepts.

One of the first cases that was discussed here illustrates an important point in this respect. In this case a woman attempted to kill her three children. In reviewing the history, one might describe this woman as homosexual, for it seems that her whole life has been an attempt to deny the reality of her own separateness and that she has been trying very hard to make herself just like some one else and to pattern her life after that person. This is particularly true in her relation to her mother. It seemed wrong for her to accept the fact that she was different from her mother; a good deal of her determination has been directed toward erasing the fact of her own difference, and a good deal of her guilt seems to have arisen because she was not able to evade that fact. Her children represented the product of her own creation, which in turn represented the fact that in herself she had creative capacities. Therefore, it was hard for her to accept these children as having any value. They symbolized her own bad self, and in her psychotic condition she attempted to destroy these symbols of her badness. In homosexuality one has the attempt of one person to live through another and to pattern himself after some one who has an organic similarity to himself; thus, it is an attempt to evade the reality of difference, and that is what this woman was trying to do.

A NEW METHOD FOR REMOVAL OF FOREIGN BODIES FROM THE GASTRO-INTESTINAL TRACT. DR. CHARLES A. LAUBACH,† Norristown, Pa. (by invitation).

A special barium preparation (bari-o-meal), which contains approximately 73 per cent of barium sulfate with the addition of special cereals, was used in the removal of foreign bodies from the gastro-intestinal tract in place of barium sulfate, which proved too constipating. The chemical properties of this substance appear to produce normal peristalsis.

When a foreign body is present in the stomach, a certain amount of the mixture is given, depending on the nature of the foreign body. This generally consists of a 50 per cent mixture with water, in a quantity of from 300 to 500 cc. When the foreign body is in the intestinal tract, smaller amounts are given at more frequent intervals. Large doses are given twice daily and are continued for several days, until fluoroscopic examination shows that the object is in the rectum or removed.

LESIONS OF THE CORPUS CALLOSUM AMONG PSYCHOTIC PERSONS. DR. THOMAS K. RATHMELL, Norristown, Pa.

Lesions of the corpus callosum present a diagnostic problem to both the neurologist and the psychiatrist. Physiologic knowledge of this structure is dependent on the experiments of Lafora and Prados and Seletskiy and Gilula on animals

† Dr. Laubach died on June 20, 1937.

and the clinical studies of Baker and Graves, Alpers and Grant and, recently, Trescher and Ford. A pathologic diagnosis of agenesis of this structure and glioblastoma multiforme was made in 2 cases in which a picture of arteriosclerosis and epilepsy with hydrocephalus was presented during life. This is the third presentation of agenesis of the corpus callosum in the American literature. Reconsideration of these cases and review of the literature led me to believe that a provisional, if not absolute, diagnosis of a lesion of the corpus callosum can be made during life. However, any clinical syndrome set up as characteristic of involvement of the corpus callosum must give consideration to the type of lesion as well as to its location, and will therefore be variable in many qualifications. Additional reports of such cases, with correlation of the clinical and pathologic observations, will add to the ability to appreciate the problem of the psychosis associated with an organic lesion of the brain.

DISCUSSION

DR. R. A. MATTHEWS: Several years ago I heard Dr. Alpers' presentation on this subject, and even at that time I was not sure that a convincing case for a syndrome of the corpus callosum had been made out. It appears that every time one tries to make a neurologic diagnosis on the basis of mental symptoms alone one gets into difficulty. Dr. E. D. Hoedemaker, of Seattle, and I made a diagnosis during life of Pick's lobar atrophy on the basis of the mental picture in 2 cases. In 1 case the condition proved to be Pick's disease, but in the other, in which almost identical mental symptoms were shown, it was something else. One must be careful in making the diagnosis of a lesion of the corpus callosum on the basis of the mental symptoms alone, for other conditions present the same picture. Dr. Rathmell's presentation was of practical interest.

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

Regular Meeting, Dec. 17, 1936

STANLEY COBB, M.D., *Presiding*

ENVIRONMENTAL STRESS AS A PRECIPITATING FACTOR FOR RHEUMATOID ARTHRITIS. DR. WALTER BAUER, DR. STANLEY COBB and MISS ISABEL WHITING.

The life charts shown are abstracts of more complete charts. Our object is to show the time relation of the attacks of arthritis, the medical data and the social data. In the ordinary case record these important relationships are lost.

The medical data were gathered from the record and by interview. The social data was obtained at one sitting by the social worker; usually the interview lasted an hour or more. Fifty cases were thus studied. In 33 there was an obvious coincidence of a pathologic social situation with the attacks of arthritis. In 7 a possible coincidence was shown, and in 10, no coincidence.

It seems fair to conclude that if in one interview a relationship between environmental factors and arthritic attacks can be found in 66 per cent of patients in an outpatient clinic, careful psychiatric study will reveal a greater percentage of relationship. The data emphasize what has long been known to clinicians: Sufferers from rheumatism must be protected from worry. However, the data also indicate that it is important for the internist to study the psychobiologic character of each sufferer from rheumatoid arthritis in order that the psychologic factor may be evaluated and treated.

A PATIENT WITH HYSTERIA. DR. MANDEL E. COHEN.

THE ACID-BASE BALANCE OF THE BLOOD IN HYSTERICAL HYPERVENTILATION. DR. JOHN H. TALBOTT and DR. FREDERICK S. COOMBS.

These two papers will be published as a combined article (Talbott, Cobb, Coombs, Cohen and Consolazio) in a later issue of the ARCHIVES.

Regular Meeting, Jan. 21, 1937

STANLEY COBB, M.D., *Presiding*

PROSTIGMIN IN THE DIAGNOSIS AND TREATMENT OF MYASTHENIA GRAVIS. DR. H. R. VIETS, DR. ROBERT S. SCHWAB and DR. ROGER S. MITCHELL.

Diagnosis.—Prostigmin (the dimethylcarbamic ester of 3-hydroxyphenyltrimethyl ammonium methylsulfate) may be used intramuscularly as an aid in the diagnosis of myasthenia gravis. Reports on this test have already been published by Viets and Schwab (*New England J. Med.* **213**:1280 [Dec. 26] 1935) and Viets and Mitchell (*New England J. Med.* **215**:1064 [Dec. 3] 1936). The drug is supplied in ampules of 0.5 mg. each, in a solution of 1:2,000. For testing, the contents of two or three ampules is injected either subcutaneously or, preferably, intramuscularly, and at the same time $\frac{1}{100}$ or $\frac{1}{150}$ grain (0.65 or 0.4 mg.) of atropine sulfate is given. The latter is usually necessary to offset the discomfort from increased peristalsis following injection of prostigmin. At stated intervals of ten and thirty minutes and one, two and four hours, and occasionally six or eight hours, after the injection, it has been found convenient to record the changes in the paralyzed muscles and the increased improvement as noted by the patient. These objective and subjective changes are now recorded on a schedule of from 1 to 4 for each period. If all the changes were maximum and a score of 4 were recorded each time, the total would be 56. The average score for patients with myasthenia gravis is about 30. The response is often rapid, and in ten minutes muscles are moved which were formerly completely paralyzed. The maximum effect occurs in from thirty minutes to one hour, and the total effect usually lasts from three to four hours, and sometimes as long as six hours. In conditions other than myasthenia gravis the average score for 27 patients was 1.5, and no score was over 4 or 5.

Treatment.—One or 2 patients have been treated with prostigmin used subcutaneously or intramuscularly. This, however, has not proved satisfactory on account of the difficulty of giving the drug in this manner. We have therefore used recently a new preparation of prostigmin in tablet form, 15 mg. in each tablet. In order to obtain an effect corresponding roughly with that produced by injection of three ampules of the solution of prostigmin, which is equivalent to 1.5 mg., it has been found necessary to give from six to nine tablets of the prostigmin orally. This amounts to between 90 and 135 mg. per day. The treatment is usually given at intervals of from two to three hours, and it has been found that one of the best methods is to give two tablets before each meal and one tablet between meals. With the use of prostigmin by mouth, moreover, it has, in most cases, been found necessary to give some form of atropine in order to overcome the disagreeable intestinal symptoms. The drug usually used is tincture of belladonna, in doses of from 5 to 15 drops three times a day. It has been suggested that the use of potassium chloride would augment or prolong the effect of prostigmin. As potassium chloride is disagreeable to take and the suggested dose is from 3 to 10 Gm. a day, we have found it convenient to put up the drug in a 25 per cent solution disguised with compound elixir of almond. One gram is contained in a teaspoonful, and from one to three teaspoonfuls can be taken three or four times a day. Although somewhat disagreeable, the drug is fairly easily tolerated.

Eight patients have been on this regimen for from three to seven months. They take from five to nine tablets of prostigmin a day by mouth. Six of the 8 patients also take tincture of belladonna, in doses which vary from 8 to 12 drops. Five of the 8 take potassium chloride, from 4 to 6 Gm. a day, and 2 of the 8, ephedrine sulfate, $\frac{1}{8}$ grain (0.0246 Gm.), three times a day. Although we have not reached a fixed standard of dosage, it is believed that all 8 patients are doing fairly well on this schedule.

STUDIES ON CHILDREN WITH BEHAVIOR PROBLEMS. DR. PHILIP SOLOMON, DR. HERBERT JASPER and DR. CHARLES BRADLEY.

We report some results of our studies on children with behavior problems at the Emma Pendleton Home, Providence, R. I. At this institution the child is placed, so far as is possible, in a normal, natural environment, with a minimum of the "institutional" atmosphere. At the same time he is provided with some of the best features of the modern home, school and hospital. A sufficiently large staff, including specialists in the fields of pediatrics, neurology, psychiatry, neurophysiology, nursing, physical and academic education, child psychology and recreation, permits a complete twenty-four hour day control of the child's activities for therapeutic and research purposes.

All behavior problems are considered as reactions between the individual child as an organism and his environment. The nature both of the organism and of the environment is important in the etiology in each case, but in some instances the organic, and in some the environmental, conditions assume the major rôle. In all cases a proper evaluation of both is attempted. The present report is concerned with the use of electro-encephalography as an aid to adequate diagnosis of the organic factors in behavior disorders.

We have made 92 complete electro-encephalographic examinations of 57 children with behavior problems. These records have been compared with those in 250 similar examinations of 112 normal subjects, 117 examinations of 53 patients with convulsive disorders and 79 examinations of 68 patients with other neuropsychiatric diseases. The method is described by Jasper and Andrews in a paper to be published in a later issue of the ARCHIVES.

Normal brain records were found for 28 of the children with behavior problems, abnormal records for 19 and questionable records for 10. The abnormalities consisted chiefly of large slow waves, sometimes regularly repeated at frequencies of from 2.5 to 6 or 7 per second and sometimes irregularly repeated but of long duration, occurring almost continuously and interrupting at intervals what would otherwise be a normal record. A given subject often gave pathologic (P) waves with wide variations in frequency, merging into the normal alpha rhythm of from 8 to 13 per second. A common frequency of the slow waves of large amplitude was from 3 to 4 per second, which definitely relates the condition to the convulsive states, in which such frequencies are always found. In some of our cases the presence of a large number of these waves was associated with borderline convulsive states, and in some, even with mild seizures which had previously been unrecognized.

In 10 of the 19 patients who had abnormal records a fairly characteristic clinical picture was present, namely, marked hyperactivity, impulsiveness, irritability and extreme variability in behavior from time to time without apparent reason. The variability was especially noticeable in school, where these children learned well on some days and almost not at all on others. It was thought that this type of behavior could be correlated with the presence of the P waves in the electro-encephalographic record, since these waves were much more numerous on "bad" than on "good" days. In only 3 of the children with normal electro-encephalographic records was behavior similar to this present.

In 22 of the total group of children with behavior problems, there was clinical cause for the suspicion of pathologic conditions in the central nervous system, of whom 14 had abnormal and 8 normal electro-encephalograms. The pathologic conditions included encephalitis, congenital defect, cerebral trauma, cerebral vascular accident and prolonged attacks of asphyxia (laryngismus stridulus in 1 case, and severe asthma in another).

Eighteen of the children with behavior problems were considered to have essentially recovered at the time the electro-encephalograms were taken. It is interesting to note that 5 of these were in the group who had abnormal electro-encephalograms. This fact indicates that with proper training some children with behavior problems can learn to make a good social adjustment in spite of abnormalities in the brain activity.

P waves are found in normal infancy and early childhood and during drowsiness, normal sleep and hyperventilation. Acute conditions which produce P waves are severe alcoholism, anesthesia, effects of various other drugs (barbiturates, morphine and evipal [sodium n-methylcyclohexenylmethylmelonylurea]), anoxemia, insulin shock, increased intracranial pressure, carbon monoxide poisoning and meningitis. Organic diseases of the nervous system in which P waves have been found are: various congenital abnormalities, encephalitis, cerebral trauma, tumor of the brain, cerebral vascular accidents, dementia paralytica, lead encephalopathy, carbon monoxide encephalopathy and Alzheimer's disease. In all the preceding normal and pathologic conditions, the changes in behavior are characterized by irritability, impulsiveness, hyperactivity and involuntary movements (including convulsions). There are also changes in mental activity characterized by dulness, confusion, absences and loss of consciousness.

The electro-encephalogram does not yield pathognomonic data with regard to the pathologic condition behind various clinical disorders, but it is an important diagnostic tool in that it gives precise information as to some aspects of disordered cortical function. For example, it shows that similar abnormalities in the electrical activity of the cortex (P waves) may be brought on by a variety of causes and that these abnormalities are associated with certain behavioral and mental changes which have much in common. The weakness of the electro-encephalographic technic for etiologic diagnosis is compensated for by the insight given into physiologic dysfunction. The diagnosis of a "behavior problem," like that of "epilepsy," is of no nosologic significance.

Book Reviews

Clinical Psychology. A Handbook of Children's Behavior Problems. By C. M. Louttit. Price, $3.50. Pp. 695, with 20 illustrations. New York: Harper & Brothers, 1936.

This book is a comprehensive and systematic presentation of the materials of clinical psychology, which the author approaches as a field of applied psychology, stressing, however, the relations of clinical psychology to medicine, education and sociology. The contents are concerned mainly with behavior problems of children; the subjects discussed include methods of diagnosis, abilities and personality and conduct disorders, as well as the psychoneuroses, psychoses and some organic disabilities. The literature has been well summarized, and the author cites numerous references to original sources. One of the difficulties with the book is that it contains too many topics. It is obvious that the author cannot discuss all of them in detailed fashion, although by the use of numerous references to other writers he gives the impression of having discussed each subject comprehensively. In many places the book appears more like a compendium than a discussion of the subject matter. The author regards behavior difficulties as primarily unacceptable habits; when children acquire such practices they need reeducation in desirable habits. In this connection he indicates the importance of a cooperative approach by the psychologist, psychiatrist and social worker in bringing about the needed reeducation. The chapter on psychoneuroses and psychoses is inadequate and oversimplified, and too many suggestions are made regarding methods of treatment in psychiatry.

Practical Examination of Personality and Behavior Disorders, Adults and Children. By Kenneth E. Appel and Edward A. Strecker. Cloth. Price $2. Pp. 219. New York: The Macmillan Company, 1936.

This book consists of two parts, the first dealing with the psychiatric examination of adults and the second with that of children. The first chapter on the art and practice of psychiatric examination is a practical and valuable article on how to handle patients with mental disturbances. It contains many useful suggestions chiefly as to how to examine patients in office practice and is therefore a useful introduction to the subject-matter handled in subsequent chapters. These chapters contain guides to direct questions and to fruitful sources of inquiry in cases of mental disease. They cover a wide variety of subjects, all of them important in the study of psychogenic disorders. That there is need for books of this sort cannot be questioned. In this volume a sincere attempt is made to bring to the medical student and physician something of the actual tools and technic of a psychiatric examination. As a laboratory guide for students and practitioners the book is satisfactory and can be highly recommended.

INDEX TO VOLUME 38

The asterisk (*) preceding the page number indicates an original article in the Archives. Subject entries are made for all articles. Author entries are made for original articles and society transactions. Book Reviews, Obituaries and Society Transactions are indexed under these headings in their alphabetical order under the letters B, O and S, respectively.

Abnormalities and Deformities: See Monsters; Twins; and under names of diseases, organs and regions, as Brain, abnormalities; Microcephaly; etc.

Abscess: See under names of organs and regions, as Brain, abscess; Cerebellum, abscess; Spinal Cord, abscess; etc.

Acalculia; congenital arithmetic disability and acalculia (Henschen), 634

Accidents, purposive, as expression of self-destructive tendencies, 160

Accommodation: See under Eyes

Acetyl-Beta-Methylcholine: See Choline and Choline Derivatives

Acetylcholine: See Choline and Choline Derivatives

Acid, Amino: See Amino-Acids

formic, in spinal fluid, new researches, 173

glycolic, metabolism in progressive muscular dystrophy, 413

lactic; carbohydrate metabolism of brain; origin of lactic acid, 1299

Phenylpyruvic: See Urine, phenylpyruvic acid

phosphocreatine and lactic acid changes in potassium chloride contracture of frog muscles in acid solutions, 618

Adenoma, change in basophil cells of pituitary gland in common to conditions which exhibit syndrome attributed to basophil adenoma, 1104

treatment of intrasellar tumors by radon, 879

Adler, A.: Vascular architecture of lesions of multiple sclerosis, *1

Adrenal Preparations, adrenalin-like action in extracts from prostatic and related glands, 639

chemistry of crystalline substances isolated from suprarenal gland, 617

responses of normal and hypophysectomized rabbits to adrenalin, 1105

Adrenalectomy: See under Adrenals

Adrenalin: See Adrenal Preparations

Adrenals, chemical studies on adrenal cortex; fractionation studies on hormone concentrates, 143

factors influencing lengths of survival following bilateral suprarenalectomy, 637

nitrogen and sulfur metabolism in suprarenalectomized rats, 638

studies in histochemistry; quantitative distribution of vitamin C in adrenal gland at various stages of development, 848

Aggression and anxiety in determination and nature of manic attacks, *71

Agnosia: See Blindness, psychic

Akinesia: See Movements

Alcohol, cerebral circulation; effect of alcohol on cerebral vessels, *321

Alcoholism: See also Korsakoff Syndrome

chronic, medullary alterations in case of, 621

etiology of polyneuritis in alcohol addict, 875

periodic, clinical and etiologic study of, 629

relationship between alcoholic intoxication and anoxemia, 847

Alexander, L.: Arterial supply of lateral parolivary area of medulla oblongata in man, *1243

Allen, T. P.: Calcium therapy in hypertonic colopathy; clinical observations, 179

Alpers, B. J.: Relation of hypothalamus to disorders of personality; report of case, *291

Alzheimer's Disease: See Insanity, presenile

Amaurosis: See Blindness

Amblyopia: See Blindness

Amentia: See Feeblemindness; Insanity; Mental Diseases; etc.

American Board of Psychiatry and Neurology, Inc., certification by, 1062

Amino-Acids, form of chronic epidemic encephalitis simulating Landouzy-Dejerine type of progressive muscular dystrophy; value of studies on creatine in conjunction with ingestion of amino-acid as aid in differential diagnosis, *1039

Amnesia, development of apparent unconsciousness during hypnotic reliving of traumatic experience, *1282

psychopathologic features of amnesic syndrome (confabulations of patients with Korsakoff's psychosis), 863

Analgesia: See Anesthesia

Anderson, J.: Method for rapid impregnation of microglia and oligodendroglia in material fixed in formaldehyde, *362

Anemia, pernicious, associated with psychoses, *348

pernicious, homonymous states in, 1315

pernicious; liver therapy for combined sclerosis, 878

survival and revival of nerve centers following acute anemia, *304

Anesthesia, electrical stimulation of cortex cerebri of cats; responses elicitable in chronic experiments through implanted electrodes, *927

schizophrenia and prolonged narcosis, 627

Aneurysm; aneurysmal dilatation of ophthalmic artery causing superior pseudohemianopic contraction of visual field, 1092

intracranial, unusual case; clinical and pathologic demonstration, 649

Angina Pectoris; genesis of multiple encephalomalacia and angina pectoris in foam formation, 1080

Angioma, cerebral; importance of cerebral angiography in their diagnosis, 175

von Hippel's disease; Lindau's disease, 872, 1095

venous, of sylvian aqueduct and fourth ventricle associated with internal hydrocephalus and mental deterioration, 428

Angyal, A.: Disturbances of activity in case of schizophrenia, *1047

Anomalies: See under names of organs and regions, as Brain, abnormalities; etc.

Anoxemia: See Oxygen, deficiency

Anthonisen, N. L.: Aggression and anxiety in determination and nature of manic attacks, *71

Anxiety and aggression in determination and nature of manic attacks, *71

"cold pressor test" in tension and anxiety; cardiochronographic study, *964

transference phenomenon in case of phobia, 1116

Aphasia, possibility of pure motor aphasia, 166

relationship of intellect to speech defect in aphasic patients, 406

visual; transitory word blindness associated with right homonymous hemianopia, 1328

Apoplexy: See Brain, hemorrhage

Apparatus, "cold pressor test" in tension and anxiety; cardiochronographic study, *964
continuous records of systolic and diastolic blood pressure, *365
device for controlled faradic stimulation, *1289
sensory functions of optic thalamus of monkey (Macacus rhesus); symptomatology and functional localization investigated with method of local strychninization, *913
Aqueduct of Sylvius: See under Brain
Arachnoid, arachnoiditis of base of brain, 1095
iodoventriculographic picture of chiasmatic arachnoiditis, 1334
meningitis serosa circumscripta spinalis (spinal arachnoiditis), 1099
Arachnoiditis: See under Arachnoid
Argyll Robertson Pupils: See under Pupils
Arithmetic: See Mathematics
Art as means of expression in some of major psychoses as applied in occupational therapy, 234
Arteries: See also Aneurysm; Arteriosclerosis; Blood pressure; Endarteritis; Pulse; Thrombosis; Vasomotor System; etc.
arterial supply of lateral parolivary area of medulla oblongata in man, *1243
carotid; cerebral degeneration with encephalographic study 8 years after common carotid ligation, 646
Cerebral: See also Brain, blood supply
cerebral; origin of posterior cerebral artery, 1067
cerebral; third artery of red nucleus, 1069
influence of sympathetic nerve fibers on coronary vessels, 1075
Arteriosclerosis, endocrine factor in pathogenesis of arterial hypertension, increased intracranial pressure, and premature arteriosclerosis; role of hypophysis, 1106
localization in vessels of brain, 154
Arteritis: See Endarteritis; Periarteritis
Arthritis, environmental stress as precipitating factor for rheumatoid arthritis, 1348
Astrocytoma, auditory hallucinations in case of astrocytoma of left temporal lobe, 167
clinicopathologic study of, *1208
relation of glioma of leptomeninges to neuroglia nests; report of case of astrocytoma of leptomeninges, 400
Ataxia, anatomic and clinical study of case of Friedreich's disease associated with mental disturbances, 1079
Atlas and Axis, fracture dislocation in region of atlas and axis with consideration of delayed neurologic manifestations and roentgenographic features, 426
Atrophy: See under names of organs and regions, as Brain, atrophy; Cerebellum; etc.
Attitudes, are attitudes biological or cultural in origin? 856
Audiometer: See Hearing, tests
Automatism, fugue reaction during course of cataphrenic episode, 163
Avitaminoses: See under Vitamins

Bacteria, Abortus and Melitense Group: See Undulant fever
Banks, T. E.: Factors producing lumbar cerebrospinal fluid pressure in man in erect posture, *1158
Bárány Test: See Ear, internal
Bardet-Laurence-Biedl-Moon Syndrome: See Laurence-Biedl Syndrome
Barney, B. F.: Anterolateral chordotomy for intractable pain of tabes dorsalis, *467
Basophilism: See under Pituitary Body
Basophils: See Pituitary Body
Bauer, W.: Environmental stress as precipitating factor for rheumatoid arthritis, 1348
Behavior, Children's: See under Children
Bender, M. B.: Defects in visual field of 1 eye only in patients with lesion of 1 optic radiation, 652
Benzedrine, hypertension produced with, 1325
Berger Rhythm: See Brain, physiology
Biemond Syndrome: See Laurence-Biedl Syndrome
Biochemistry: See Chemistry
Bladder, paralysis; abnormalities of micturition due to syphilis of nervous system, 1099
reaction to stimulation of points in forebrain and midbrain, 1295
Blindness: See also Vision
acetylcholine in tobacco amblyopia, 411
psychic; unilateral cerebral dominance as related to mind blindness; minimal lesion capable of causing visual agnosia for objects, *108
Word Blindness: See Aphasia, visual
Blood, diastase; comparative studies on diastase in serum and spinal fluid, 1323
Diseases: See Anemia; etc.
fats and lipoids; blood phospholipid as transport mechanism, 848
hematology of convulsions, 872
lipase, experimental studies in multiple sclerosis, *288
phosphates, relation to parathyroid tetany, 639
pressure; "cold pressor test" in tension and anxiety; cardiochronographic study, *964
pressure; continuous records of systolic and diastolic blood pressure, *365
pressure; effect of ergotamine tartrate on pressure of spinal fluid and blood during migraine headache, 172
pressure; effect of increased intracranial venous pressure on pressure of spinal fluid, 641
pressure, effect of injecting certain electrolytes into cisterna magna on, 394
pressure; effect of injection of certain nitrogen-containing compounds into cisterna magna on blood pressure of dogs, 1322
pressure; effect of intravenous injections of sucrose solution (50 per cent) on spinal fluid pressure, blood pressure and clinical course in cases of chronic hypertension, 641
pressure, high; endocrine factor in pathogenesis of arterial hypertension, increased intracranial pressure, and premature arteriosclerosis; role of hypophysis, 1106
pressure, high; hypertension produced with benzedrine, 1325
pressure, high; hypertensive apoplexy and its causation, *1176
pressure, high; is resection of splanchnic nerves justified in treatment of permanent essential arterial hypertension? 1326
pressure, high; relation of basophilic cells of neurohypophysis to hypertension and eclampsia, 1108
pressure, high; relation of increased intracranial tension to arterial hypertension, 886
pressure; pressor and oxytocic fractions of posterior pituitary extract; comparative effects on blood pressure and intestinal activity, 638
sedimentation rate, significance in neurology and psychiatry, 645
sugar; clinical experience with hypoglycemic therapy of psychoses, 190
sugar; curve for sugar content following encephalography; comparison with usual curve for dextrose tolerance, *985
sugar; experiences with insulin shock therapy in schizophrenia, 907
sugar; hypoglycemic state in treatment of schizophrenia, 879
sugar; hypoglycemic treatment of psychoses, 412
sugar; hypoglycemic treatment of psychoses; experiences at Bellevue Hospital, 191
sugar in blood and spinal fluid, 173
sugar; incidence and differential diagnosis of hypoglycemic convulsions, 869
sugar; insulin hypoglycemic shock in treatment of psychotic patients, 438

Blood—Continued
sugar; origin and nature of hypoglycemic therapy of psychoses, 188
sugar; response of schizophrenic subjects to hypoglycemic insulin shock, 1325
sugar; treatment of schizophrenia by production of hypoglycemic state, 880
sugar; vegetative disturbances following encephalography, 175

Book Reviews:

Clinical Psychology: Handbook of Children's Behavior Problems; C. M. Louttit, 1352
Frigidity in Women: Its Characteristics and Treatment; E. Hitschmann and E. Bergler, 444
Guiding Your Life, with Psychology as Key; J. A. Jackson, 238
Handbuch der Neurologie: Vol. V; edited by O. Bumke and O. Foerster, 1133
Handbuch der Neurologie; Vol. VIII; edited by O. Bumke and O. Foerster, 1134
Intellectual Functions of Frontal Lobes: Study Based upon Observation of Man After Partial Bilateral Frontal Lobectomy; R. M. Brickner, 236
Kriminalpsychopathologie und psychobiologische Verbrecherkunde; K. Birnbaum, 443
Lehrbuch der forensischen Psychiatrie für Aerzte, Juristen und höhere Beamte des Sicherheitsdienstes; R. Michel, 443
Objective and Experimental Psychiatry; D. E. Cameron, 238
Ocular Fundus in Diagnosis and Treatment; D. T. Atkinson, 1134
Otologische Diagnostik der Hirntumoren; H. Brunner, 666
Practical Examination of Personality and Behavior Disorders, Adults and Children; K. E. Appel and E. A. Strecker, 1352
Psychogenic Tonsillitis; R. Bilz, 1132
Psychology of Adjustment: Objective Approach to Mental Hygiene; L. F. Shaffer, 912
Réactions labyrinthiques et équilibre; G. G. J. Rademaker, 441
Ueber die Erkennung der traumatischen Hirnverletzung; E. Grunthal, 1131
Vom Sinn der Sinne; E. Straus, 1130

Boshes, B.: Carbohydrate metabolism in epilepsy, 229
Bouckaert, J. J.: Survival and revival of nerve centers following acute anemia, *304
Bourneville's Disease: See Sclerosis, tuberous
Boutons Terminaux: See under Spinal Cord
Bradley, C.: Studies on children with behavior problems, 1350
Brain: See also Cerebellum; Corpus Callosum; Corpus Striatum; Hypothalamus; Medulla Oblongata; Meninges; Nervous System; Pons Varolii; Thalamus; etc.
abnormalities; congenital malformation of cerebrum associated with microcephaly, 152
abscess of undetermined etiology; report of 4 cases in which recovery occurred, 1124
abscess; removal in mass of subacute abscess of cerebral hemispheres without drainage, 635
and endocrine glands in old age, 640
angiomas; importance of cerebral angiography in their diagnosis, 175
arachnoiditis of base of brain, 1095
atrophy; acquired dementias, 162
atrophy; bilateral atrophic lobar sclerosis following thrombosis of superior longitudinal sinus, 1078
atrophy of parietal and cerebellar lobes associated in certain cases with multiple sclerosis, 218
atrophy; psychopathology of Pick's disease, *473
Blood Supply: See also Arteries, cerebral
blood supply; endocranial blood vessels of Amblystoma tigrinum, 844

Brain—Continued
blood supply; necrotizing encephalitis simulating tumor of brain clinically and due to necrotizing angiitis; clinicopathologic report, *775
blood supply; variability of perivascular reactions in different types of encephalitis, 403
carbohydrate metabolism; determination of glycogen in nerve tissue, 1071
carbohydrate metabolism; effect of varying carbohydrate and insulin supply on glycogen, free sugar, and lactic acid in mammalian brain, 617
carbohydrate metabolism; origin of lactic acid, 1299
circulation; effect of alcohol on cerebral vessels, *321
changes in plexectomized dogs with comments on spinal fluid, *1224
comparative cytoarchitectonic study of motor and premotor areas in primate cortex, 613
connections between striatum and substantia nigra in, *550
cortical area concerned with coordinated walking in rat, 844
cortical innervation of respiratory movements; slowing of respiratory movements by cerebral stimulation, 397
cortical sensory disturbances in man, 1074
corticifugal fiber connections of cortex of Macaca mulatta; frontal region, 390
corticifugal fiber connections of cortex of Macaca mulatta; occipital region, 390
corticifugal fiber connections of cortex of Macaca mulatta; parietal region, 391
corticifugal fiber connections of cortex of Macaca mulatta; temporal region, 391
cystic ependymocytoma of third ventricle, 153
cystic tumor of third ventricle containing colloid material, *268
cysts, neuro-epithelial, of third ventricle, 400
cysts, neuro-epithelial, of third ventricle; report of case with recovery following operation, *1055
degeneration with encephalographic study 8 years after common carotid ligation, 646
device for controlled faradic stimulation, *1289
diffuse changes in poisoning with oil of chenopodium, 1304
Diseases: See also Encephalitis; Insanity; Mental Diseases; etc.
diseases; significance of frontal lobes for mental performances, 1087
diseases; symptomatology of disorders of frontal lobe, 1099
disorders of motor function following ablation of part of "leg area" of cortex in man, 407
effect of experimental lesions of cortex on "psychogalvanic reflex" in cat, *308
effect of injections of colloidal thorium dioxide on ventricles and subarachnoid spaces, *340
effect of roentgenotherapy on gliomas, *513
efferent fibers of frontal lobe of monkey, Macaca mulatta, 1065
electrical stimulation of cortex cerebri of cats; responses elicitable in chronic experiments through implanted electrodes, *927
excision of speech area without resultant aphasia, 430
fiber tract from lamina terminalis in birds, 1296
Georgetown University Brain Research Institute, 1063
gliomas, 854
hemorrhage; hypertensive apoplexy and its causation, *1176
hemorrhage into floor of fourth ventricle in intoxications and inflammations of brain, 1308
histologic changes in hypothalamus, substantia nigra and inferior olive in epilepsy, 856

Brain—Continued
histology of paraphysis of Amblystoma, 614
hyperostosis frontalis interna; degenerative disease of brain, 658
Inflammation: See Encephalitis
Injuries: See also Head, injuries
injuries; diffuse cortical contusion of occipital lobe, 151
injuries; late injury of human brain resulting from roentgen irradiation, 154
is all colloid observed in midbrain of hypophysial origin? 1297
localization of function; central path of light reflex, 843
localization of function; frontal lobe and equilibrium, 147
localization of function; functional determinants of cerebral localization, *371
localization of function; specific responses elicitable from subdivisions of motor cortex of cerebrum of cat, 614
membranous parts of brain, meninges and their blood vessels in Amblystoma, 844
nucleus of posterior longitudinal bundle, fibers arising therefrom and probable relation of both to automatic posture of head, 1297
ontogenesis of isocortex in man, 1070
optic connections of diencephalon and midbrain of cat, 391
pathology; genesis of multiple encephalomalacia and angina pectoris in foam formation, 1080
pathology; prevention of nutritional encephalomalacia in chicks by vegetable oils and their fractions, 1076
pathology; relation of handedness to language mechanism, 405
pathology; ulceration in digestive tract of dog following intracranial procedures, 395
physiological study of cerebral motor cortex and control of posture in sloth, 143
physiology; Berger rhythm in monkey's brain, 1301
physiology; dissociation of cortical excitation from cortical inhibition by pyramid section and syndrome of that lesion in cat, 144
physiology; electro-encephalograms in man, 398
physiology; electro-encephalography in diagnosis and localization of intracranial lesions, 659
physiology; extent and structure of electrically excitable cerebral cortex in frontal lobe of dog, 392
physiology; fundamental effects of epileptogenous agents on central nervous system, 394
physiology; origin of Berger rhythm, 145
physiology; spread of activity in cerebral cortex, 850
poverty of medullary sheath in central vegetative structures of, 1296
primary melanosarcoma, numerous pigmented nevi of skin and extensive neurofibromatosis of cutaneous nerves, 621
processes of localization in developing Fundulus, 845
reaction of bladder to stimulation of points in forebrain and midbrain, 1295
roentgenography; akinetic states following introduction of air into third ventricle and their significance, 175
roentgenography; curve for sugar content of blood following encephalography; comparison with usual curve for dextrose tolerance, *985
roentgenography; electrocardiographic changes during encephalography, 644
roentgenography; encephalogram in epilepsy, 1335
roentgenography; encephalographic findings in dementia praecox, 439
roentgenography; encephalography with ethylene, 1333
Brain—Continued
roentgenography; iodoventriculographic picture of chiasmatic arachnoiditis, 1334
roentgenography; pneumencephalographic diagnosis of tumors of corpus callosum, 647
roentgenography; roentgenoscopic examination of ventricular cavities with iodized oil (roentgeniodoventriculoscopy), 647
roentgenography; social prognosis of schizophrenia on basis of encephalographic findings, 862
roentgenography; vegetative disturbances following encephalography, 175
selective involvement of layers of cerebral cortex in mental disease, 1306
size and mentality, 1086
subcortical prefrontal lobotomy in treatment of certain psychoses, 225
subthalamus and structures of subthalamo-mesencephalic region, 393
surgery; effects of occipital lobectomy on vision in chimpanzee, 415
Syphilis: See Syphilis
tumor syndrome with hyperthermia and visceral disorders due to chronic basilar tuberculous meningo-encephalitis, 166
tumors; auditory hallucinations in case of astrocytoma of left temporal lobe, 167
tumors; cerebral syphilis and glioma, 1094
tumors; clinicopathologic study of astrocytomas, *1208
tumors; defects in visual field of 1 eye in patients with lesion of 1 optic radiation, 652
tumors; differential diagnosis of tumor of brain and "pseudotumoral" encephalitis, 1094
tumors; effects of roentgen therapy on gliomas, 879
tumors; homonymous hemianopia; practical points in interpretation with report of 49 cases in which lesion in brain was verified, 881
tumors in monkey, 154
tumors; masked epilepsy and simulation of traumatic epilepsy by cerebral tumor with reference to head injuries without fracture, 872
tumors, multiple metastatic, arising from primary bronchial carcinoma, 1305
tumors, multiple primary, 399
tumors; relation of hypothalamus to disorders of personality; report of case, *291
tumors; sense of smell; localization of tumors of frontal lobe of brain by quantitative olfactory tests, 644
tumors; value of indirect roentgenologic signs in diagnosis of, 1334
unilateral cerebral dominance as related to mind blindness; minimal lesion capable of causing visual agnosia for objects, *108
venous angioma of sylvian aqueduct and fourth ventricle associated with internal hydrocephalus and mental deterioration, 428
vitamin B_1 deficiency in rat's brain, 397
Bromide, intoxication, chronic, halide distribution in body fluids in, 396
intoxication, with symptomatic psychoses, 1084
psychosis, 50 cases of, 653
Bronchi, cancer; multiple metastatic tumors in brain arising from primary bronchial carcinoma, 1305
Buchanan, A. R.: Secondary vestibular fibers and medial longitudinal bundle, 660
Buchanan, D. N.: Chronic tetanus (presentation of patient), 1118

Cachexia, Pituitary: See Pituitary Body, diseases
Calcium, effect of liberal intakes of calcium or calcium and phosphorus on growth and body calcium, 1299
therapy in hypertonic colopathy; clinical observations, 179
Calvarium: See under Cranium

Canavan, M. M.: Enostoses within calvarium; survey of skulls in Warren Museum of Harvard University Medical School, *1249
Cancer: See also Tumors; etc.; and under names of organs and regions, as Bronchi, cancer; Prostate, cancer; etc.
cells in spinal fluid, 1080
Carbohydrates: See also Dextrose; Glycogen; etc.
metabolism in epilepsy, 229
metabolism of brain; effect of varying carbohydrate and insulin supply on glycogen, free sugar, and lactic acid in mammalian brain, 617
metabolism of brain; origin of lactic acid, 1299
Carbon dioxide, word associations as affected by deficient oxygen, excess of carbon dioxide and hyperpnea, *491
Cardiovascular System: See Arteries; Heart; Vasomotor System; etc.
Carmichael, E. A.: Factors producing lumbar cerebrospinal fluid pressure in man in erect posture, *1158
Carotid Sinus, association of carotid sinus reflexes with syncope and convulsions; report of 4 cases, *761
effect on venous flow, 1301
Case, T. J.: Electro-encephalography in diagnosis and localization of intracranial lesions, 659
Cataphrenia: See under Mental Diseases
Cataract, psychoses complicating recovery from extraction of, *818
Catatonia: See under Dementia Praecox
Cauda Equina: See Spinal Cord
Cave, H. A.: Contribution to history of narcolepsy, *136
Cavernous Sinus; multiple orbitocranial lesions from lead shot; syndrome of hemorrhage of cavernous sinus, 165
Cells: See also Cancer, cells; Neuroglia; Tissue; etc.
consideration of biological factors influencing radiosensitivity of, 617
division and differentiation in growth of specialized vertebrate tissues, 1067
presence of colloid inclusions in ganglion cells of human medulla oblongata, 846
Cephalalgia: See Headache
Cerebellum, abscess of, 420
anatomic and clinical study of case of Friedreich's disease associated with mental disturbances, 1079
atrophy of parietal and cerebellar lobes associated in certain cases with multiple sclerosis, 218
diffuse sclerosis of, 622
function from clinical standpoint, 422
olivocerebellar atrophy, 1305
review and interpretation, *580
Cerebrospinal Fluid: See also Meninges, permeability; Spinal Puncture; etc.
Ayala index; preliminary report, 437
biologic properties in schizophrenia, supplementary report, 173
carcinomatous cells in, 1080
changes in brain in plexectomized dogs with comments on, *1224
cholesterol content, investigations of, 645
comparative studies on diastase in serum and spinal fluid, 1323
cranial venous sinuses; correlation between skull markings and roentgenograms of occipital bone, 647
effect of ergotamine tartrate on pressure of spinal fluid and blood during migraine headache, 172
effect of intravenous injections of sucrose solution (50 per cent) on spinal fluid pressure, blood pressure and clinical course in cases of chronic hypertension, 641
factors producing lumbar spinal fluid pressure in man in erect posture, *1158
in vascular diseases of central nervous system, 641
Cerebrospinal Fluid—Continued
new researches on formic acid in, 173
physiopathologic changes in intracranial pressure associated with production and resorption of, 643
pressure, effect of increased intracranial venous pressure on, 641
relation to polyneuritis, 174
sugar in blood and spinal fluid, 173
sugar, significance of diminution in tuberculous meningitis, 865
variations of cranial venous sinuses in region of torcular herophili, 632
Cerebrum: See Brain
Character, treatment with acetylcholine for certain character changes in children with tendency to impulsive behavior, 1325
Charcot's Joints: See under Tabes Dorsalis
Chase, W. H.: Hypertensive apoplexy and its causation, *1176
Chemistry, evaluation of biochemical approach to psychoses, 207
Chenopodium, diffuse cerebral changes in poisoning with oil of chenopodium, 1304
Chiasm, Optic: See Optic Chiasm
Children, behavior, personality and intelligence of children with endocrine disturbances, 1339
development of language function in, 1340
treatment with acetylcholine for certain character changes in children with tendency to impulsive behavior, 1325
with behavior problems, studies on, 1350
Chlorides, halide distribution in body fluids in chronic bromide intoxication, 396
Choked Disk: See Neuritis, optic
Cholesteatoma, dermoid and epidermoid tumors (cholesteatomas) of central nervous system, 870
Cholesterol content of muscle, 847
in Cerebrospinal Fluid: See Cerebrospinal Fluid, cholesterol
provitamin D of heat-treated cholesterol, 396
Choline and Choline Derivatives, acetylcholine in tobacco amblyopia, 411
chemical transmission of excitation from motor nerve to voluntary muscle, 849
physiologic effects of acetyl-beta-methylcholine (mecholyl) and its relationship to other drugs affecting autonomic nervous system, 1298
Chondroma, spinal compression caused by ecchondrosis of intervertebral fibrocartilage, 1316
Chor, H.: Water metabolism in relation to convulsions, *798
Chordotomy: See Spinal Cord, surgery
Chorea; constitutional aspects of chorea and its sequelae, 1315
Huntington's, genealogical study, 910
Choriomeningitis: See Meningitis
Choroid Plexus, changes in brain in plexectomized dogs with comments on spinal fluid, *1224
tumors in childhood, 851
Chromatophore: See under Melanin, pigmentation
Chronaxia, isolated electric stimulation of 2 vestibular nerves; double chronaxia on each side, 883
obliterating arteritides; estimation of function by measurement of chronaxia, 645
Cisterna Magna, Injections into: See Electrolytes; Nitrogen
Clark, S. L.: Electrical stimulation of cortex cerebri of cats; responses elicitable in chronic experiments through implanted electrodes, *927
Cobb, S.: Environmental stress as precipitating factor for rheumatoid arthritis, 1348
Cochlea: See Ear, internal
Cohen, B.: Repression and communicability in catatonic stupor, *572
Cold; "cold pressor test" in tension and anxiety; cardiochronographic study, *964

Colon, calcium therapy in hypertonic colopathy; clinical observations, 179
Communism, sociological significance of, considered in light of psychoanalysis, 1085
Constipation, relation of persecutory delusions to functioning of gastro-intestinal tract, 857
Constitution; constitutional aspects of chorea and its sequelae, 1315
constitutional aspects of paranoid reactions, 205
constitutional relationship between tuberculosis and mental disease, 630
Contractures, extreme encephalitic parkinsonism with contractures which relax during somnambulistic state, 166
Contusions: See Brain, injuries
Convulsions: See also Epilepsy
association of carotid sinus reflexes with syncope and convulsions; report of 4 cases, *761
histologic changes in insulin convulsions, 856
hypoglycemic, incidence and differential diagnosis of, 869
water metabolism in relation to, *798
Corpus Callosum, lesions among psychotic persons, 1347
tumors, mental syndrome of, 870
tumors, pneumencephalographic diagnosis of, 647
Corpus Luysi: See Hypothalamus
Corpus Striatum, connections between striatum and substantia nigra in human brain, *550
état marbré, 852
tuberculous encephalitis of striatum associated with parkinsonian syndrome, 867
Corrin, K. M.: Mechanism of grand mal convulsion; preliminary report, 890
Cranium: See also Frontal Bone
blood supply; physiopathologic changes in intracranial pressure associated with production and resorption of spinal fluid, 643
cranial venous sinuses; correlation between skull markings and roentgenograms of occipital bone, 647
craniograms, 1335
enostoses within calvarium; survey of skulls in Warren Museum of Harvard University Medical School, *1240
Injuries: See Brain, injuries; Head, injuries
multiple orbitocranial lesions from lead shot; syndrome of hemorrhage of cavernous sinus, 165
pressure; endocrine factor in pathogenesis of arterial hypertension, increased intracranial pressure, and premature arteriosclerosis; role of hypophysis 1106
pressure, intracranial, in head injuries, 869
pressure; relation of increased intracranial tension to arterial hypertension, 886
tumors; case of intracranial epidermoid, 177
variations of cranial venous sinuses in region of torcular herophili, 632
Creatine and Creatinine; form of chronic epidemic encephalitis simulating Landouzy-Dejerine type of progressive muscular dystrophy; value of studies on creatine in conjunction with ingestion of amino-acid as aid in differential diagnosis, *1039
studies in diseases of muscle; metabolism of creatine and creatinine in progressive muscular dystrophy, *992
Crime and Criminals: See also Delinquency; Jurisprudence, Medical
classification of felons in midwestern state penitentiary, 1082
psychology of prison language, 1081
Curare, depressant peripheral effect of prostigmin and its temporary antagonism by curarine, 1300
Curran, F. J.: Study of 50 cases of bromide psychosis, 653
Cushing Syndrome: See under Pituitary Body
Cysts: See under names of organs and regions, as Brain; etc.

Darrow, C. W.: Continuous records of systolic and diastolic blood pressure, *365
Davison, C.: Combined system disease in tabes dorsalis, *43
Encephalitis following German measles, 650
Poikilothermia with hypothalamic lesions; clinicopathologic study, *1271
Deafness: See also Hearing
neuralgias and ear symptoms, associated with disturbed function of temporomandibular joint, 874
psychotherapy in cases of suspected organic defects in young children, 1342
reaction of cochlear nerve to destruction of its end organs; study on deaf albino cats, 613
Dean, S. R.: Form of chronic epidemic encephalitis simulating Landouzy-Dejerine type of progressive muscular dystrophy; value of studies on creatine in conjunction with ingestion of amino-acid as aid in differential diagnosis, *1039
Death, lethal power of emotions, 155
Degeneration, hyaline; change in basophil cells of pituitary gland in common to conditions which exhibit syndrome attributed to basophil adenoma, 1104
Dejerine-Sottas' Disease: See Neuritis, interstitial
Delinquency, classification of defective delinquents, 1082
juvenile, and mental retardation, 1310
study of runaways at state correctional school for boys, 1083
Delusions: See Insanity, delusional
Dementia, acquired, 162
Dementia Paralytica, acute cystic pneumococcic meningitis in patient with, 401
anatomic explanation of dysarthria associated with, 873
investigations on problems of immunity against Spirochaeta pallida in general paralytics treated with malaria, 1078
Lissauer's; study of its pathogenesis, *27
permeability of meninges to arsenic in cases of dementia paralytica before and after malaria therapy, 165
psychology of juvenile paretic neurosyphilis, 858
Dementia Praecox, biologic properties of spinal fluid in schizophrenia, supplementary report, 173
disturbances of activity in case of schizophrenia, *1047
encephalographic findings in, 439
experiences with insulin shock therapy in schizophrenia, 907
hypoglycemic state in treatment of schizophrenia, 879
incidence of pulmonary tuberculosis in schizophrenic patients during period of 5 years in Ypsilanti State Hospital, 440
influence of chronic epidemic encephalitis on schizophrenia, 1088
introjection and schizophrenia, 157
new researches on formic acid in spinal fluid, 173
organic alterations in schizophrenia, 862
oxygen metabolism in schizophrenia, *1261
pure intermittent catatonia lasting 24 years, 628
repression and communicability in catatonic stupor, *572
response of schizophrenic subjects to hypoglycemic insulin shock, 1325
schizoid personality, 864
schizophrenia and prolonged narcosis, 627
schizophrenia in boy 4 years old, 632
"sex hormones" and their relation to schizophrenia, 234
social prognosis of schizophrenia on basis of encephalographic findings, 862
treatment of schizophrenia by production of hypoglycemic state, 880
vegetative nervous system in, 640
Depersonalization: See under Personality

Depression: See also Insanity; Melancholia
hematoporphyrin treatment of melancholia and endogenous depressions, 412
prognosis of depressions of later life, 1314
De Ronde, M.: Sense of guilt and need for punishment, 1344
Dextrose, curve for sugar content of blood following encephalography; comparison with usual curve for dextrose tolerance, *985
Diabetes Mellitus: See also Blood sugar
changes in spinal cord in; report of case with autopsy, *564
neuritic manifestations in, 408
Diastase in Blood: See Blood, diastase
Dictaphone; dictaphonic reproduction in case of depersonalization, 429
Diencephalon: See Brain
Diplegia: See Paralysis
Disk, Choked: See Neuritis, optic
Diuresis and Diuretics, effect of pituitary (posterior lobe) extract upon urinary flow, 1105
Dorrance, G. M.: Injection of alcohol into gasserian ganglion, 214
Dozier, P. C.: Development of language function in children, 1340
Dreams, importance of dream-analysis for psychological development, 860
in which dreamer knows he is asleep, 1082
Drugs, effects of sodium amytal and other drugs on reactivity of hypothalamus of cat, 224
effects on transmission from nerve to voluntary muscle and accommodation to different rates of destruction of chemical transmitter, 849
Ductless Glands: See Endocrine Glands
Duel, A. B.: Facial tic in relation to injury of facial nerve; experimental study, *1190
Dunn, W. H.: Evaluation of biochemical approach to psychoses, 207
Dusser de Barenne, J. G.: Sensory functions of optic thalamus of monkey (Macacus rhesus); symptomatology and functional localization investigated with method of local strychninization, *913
Dyke, C. G.: Results of roentgen treatment of tumor of pituitary gland; report on 81 patients, 48 of whom were treated exclusively by irradiation, 903
Dysarthria: See Speech, defects
Dyskinesia: See Movements
Dyspituitarism: See Pituitary Body
Dystrophy, muscular; form of chronic epidemic encephalitis simulating Landouzy-Dejerine type of progressive muscular dystrophy; value of studies on creatine in conjunction with ingestion of amino-acid as aid in differential diagnosis, *1039
muscular; metabolism of glycolic acid in progressive muscular dystrophy, 413
muscular, progressive, pathogenesis of, 414
muscular; studies in diseases of muscle; metabolism of creatine and creatinine in progressive muscular dystrophy, *992

Ear: See also Deafness; Mastoid; etc.
Internal: See also Equilibrium; Nystagmus; Reflex, aural
internal; pointing test, 883
internal; relations between cochleovestibular system and oculomotor system in case of posttraumatic paralysis of ocular muscles, 169
noises in ear, tinnitus and elementary, common and verbal auditory hallucinations, 1330
Ecchondroma: See Chondroma
Eclampsia, relation of basophilic cells of neurohypophysis to hypertension and eclampsia, 1108
Ectoderm, developmental pattern on ectodermal placodes in Rana pipiens, 1065
Electrocardiogram: See Heart, electrocardiography
Electro-Encephalography: See Brain, physiology
Electrolytes, effect of injecting certain electrolytes into cisterna magna on blood pressure, 394
Electromyogram: See under Muscles
Embolism, genesis of multiple encephalomalacia and angina pectoris in foam formation, 1080
Emotions: See also Anxiety; etc.
aggression and anxiety in determination and nature of manic attacks, *71
lethal power of, 155
logic of emotions and its dynamic background, 159
proposed mechanism of, *725
Encephalitis: See also Encephalomyelitis; Meningo-Encephalitis
acute epidemic, clinical study of 160 cases, 868
chronic epidemic, form simulating Landouzy-Dejerine type of progressive muscular dystrophy; value of studies on creatine in conjunction with ingestion of amino-acid as aid in differential diagnosis, *1039
chronic epidemic, influence on schizophrenia, 1088
chronic, symptomatic treatment with benzedrine sulfate, 892
differential diagnosis of tumor of brain and "pseudotumoral" encephalitis, 1094
epidemic; follow-up study of 266 cases, *1135
extreme encephalitic parkinsonism with contractures which relax during somnambulistic state, 166
following German measles, 650
histopathologic alterations in case of buccolingual spasm of postencephalitic origin, 1080
myxedema, acromegaly, infundibulotuberal syndrome, melancholic delirium, oneirism, ligneous thyroiditis, pituitary adenoma and pedunculo-mesodiencephalic encephalitis, 1105
necrotizing, simulating tumor of brain clinically and due to necrotizing angiitis; clinicopathologic report, *775
occurrence of epidemic encephalitis combined with multiple sclerosis, 621
of brain stem associated with gonococcic disease, 168
periaxialis diffusa; familial Schilder's disease, 1077
psychopathology and treatment of parkinsonian syndrome and other post-encephalitic sequelae, 1324
variability of perivascular reactions in different types of, 403
Encephalography: See Brain, roentgenography
Encephalomyelitis complicating measles, *1025
disseminated; histologic syndrome associated with thrombosis of small cerebral vessels, 1127
relation between disseminated nonsuppurative encephalomyelitis and multiple sclerosis, 624
Encephalopathy: See under Brain
Encephalorrhagia: See Brain, hemorrhage
Endarteritis obliterans; obliterating arteritides; estimation of function by measurement of chronaxia, 645
Endocrine Glands: See also Hormones; and under names of glands
and brain in old age, 640
and experimental epilepsy, 1075
behavior, personality and intelligence of children with endocrine disturbances, 1339
myxedema, acromegaly, infundibulotuberal syndrome, melancholic delirium, oneirism, ligneous thyroiditis, pituitary adenoma and pedunculo-mesodiencephalic encephalitis, 1105
Endocrine Therapy: See under names of glands and hormones, as Adrenal Preparations; Insulin; Pituitary Preparations
Endolymphatic organs; chemical analysis of otoliths and endolymphatic sac deposits in Amblystoma tigrinum, 612
Endothelioma, primary tumor of optic nerve, 400

Enostosis: See under Cranium
Environment, environmental stress as precipitating factor for rheumatoid arthritis, 1348
Ependymocytoma, cystic, of third ventricle, 153
Epidermoid: See Cranium, tumors
Epilepsy: See also Convulsions; Sclerosis, tuberous
carbohydrate metabolism in, 229
electro-encephalography in diagnosis and localization of intracranial lesions, 659
encephalogram in, 1335
epileptiform convulsions from "remote" excitation, *259
experimental, and endocrine glands, 1075
fundamental effects of epileptogenous agents on central nervous system, 394
hematology of convulsions, 872
hereditary factor in, 171
histologic changes in hypothalamus, substantia nigra and inferior olive in, 856
masked epilepsy and simulation of traumatic epilepsy by cerebral tumor with reference to head injuries without fracture, 872
mechanism of grand mal convulsion; preliminary report, 890
mode of onset, *744
myoclonic, of Unverricht; report of 2 familial cases, 1093
myoclonic, unusual case of, 896
new problems in humoropathologic changes in convulsive states, 1076
pathologicoanatomic changes in, 1307
pharmacologic studies of basic factors involved in treatment with borates, 880
relationship of autonomic nervous system to pathogenesis of, *16
traumatic, 167
water metabolism in relation to convulsions, *798
Epinephrine: See Adrenal Preparations
Epithelioma, unilateral global paralytic syndrome of 12 cranial nerves, 170
Equilibrium: See also Cerebellum; Nystagmus; Otolith Apparatus; Posture; Reflex, aural; etc.
and frontal lobe, 147
position of feet in station of man; relations of these phenomena to state of vestibular apparatus, 150
Erickson, M. H.: Development of apparent unconsciousness during hypnotic reliving of traumatic experience, *1282
Erotism: See under Sex
Erythema nodosum, meningeal reaction in, 868
Estrin: See Hormones, sex
État Marbré: See Corpus Striatum; Thalamus
Ethylene, encephalography with ethylene, 1333
Exophthalmos, unilateral, produced by meningioma of middle cranial fossa, 405
Extremities, limb movements studied by electrical stimulation of nerve roots and trunks in Ambiystoma, 612
Paralysis: See Poliomyelitis
vasomotor responses in hemiplegic patients, 1299
Eyes: See also under Orbit; Vision; and under special structures of eyes, i.e., Macula Lutea; Retina; etc.
diseases; visual hallucinations and lesions of visual apparatus, 418
innervation of muscle of accommodation in eye of teleost, Holocentrus, 1066
ocular complications of cerebrospinal meningitis, 164
paralysis; congenital familial ophthalmoplegia, 420
paralysis; relations between cochleovestibular system and oculomotor system in case of posttraumatic paralysis of ocular muscles, 169

Faistein, E. I.: Huntington's chorea; genealogical study, 910
Farber, S.: Survival and revival of nerve centers following acute anemia, *304
Fasting, quantities of protein lost by various organs and tissues of body during fast, 847
Fay, T.: New method of treatment for acute postoperative and posttraumatic psychoses, 1336
Feeblemindedness: See also Idiocy; Laurence-Biedl Syndrome
brain size and mentality, 1086
classification of defective delinquents, 1082
mental retardation and juvenile delinquency, 1310
phenylpyruvic oligophrenia; introductory study of 50 cases of mental deficiency associated with excretion of phenylpyruvic acid, *944
Fellowships, appointments to and opportunities for, 1063
Fender, F. A.: Device for controlled faradic stimulation, *1289
Epileptiform convulsions from "remote" excitation, *259
Fetterman, J. L.: Mode of onset of epilepsy, *744
Fever: See also Temperature; etc.
problem of long-continued, low grade fever, 857
Therapeutic: See under Dementia Paralytica; Syphilis; etc.
tumor syndrome with hyperthermia and visceral disorders due to chronic basilar tuberculous meningo-encephalitis, 166
Filum Terminale: See Spinal Cord
Fisher, C.: Hypothalamic regulation of temperature in monkey, *445
Pars nervosa of hypophysis, 1120
Flatau-Schilder's Disease: See Encephalitis periaxialis diffusa
Foot, position of feet in station of man; relations of these phenomena to state of vestibular apparatus, 150
Foreign Bodies, meningeal mesenchymoma of foreign body origin, 623
new method for removal from gastro-intestinal tract, 1347
Fray, W. W.: Roentgenologic study of orientation of pineal body; comparison of proportional and graphic method in absence of tumor of brain, *1199
Freedberg, A. S.: Association of carotid sinus reflexes with syncope and convulsions; report of 4 cases, *761
Freeman, W.: Effect of injections of colloidal thorium dioxide on ventricles and subarachnoid spaces, *340
Subcortical prefrontal lobotomy in treatment of certain psychoses, 225
Freud, Sigmund, as neurologist, 654
Friedfeld, L.: Encephalitis following German measles, 650
Friedman, E. D.: Poikilothermia with hypothalamic lesions; clinicopathologic study, *1271
Friedreich's Ataxia: See under Ataxia
Frontal Bone, hyperostosis frontalis interna, 1094
hyperostosis frontalis interna; degenerative disease of brain, 658
internal frontal hyperostosis; report of 4 new cases, 1334
osteomyelitis, notes on 3 cases, 1091
Fry, W. E.: Subarachnoid hemorrhage with reference to papilledema; experimental and clinical study, 217

Gammon, G. D.: Use of prostigmin as diagnostic test of myasthenia gravis, 890
Ganglion: See also Gasserian ganglion; Nervous System; Neurons
action potential of superior cervical ganglion, 618
anatomic and clinical study of case of Friedreich's disease associated with mental disturbances, 1079

Ganglion—Continued
Nodose: See Neurons
spinal; changes in spinal cord and posterior root ganglions in sepsis, 1102
spinal; polyradiculoganglionitis of Landry's type in syphilitic patient, 1321
Ganglionectomy: See Sympathectomy
Gardner, W. J.: Neuro-epithelial cyst of third ventricle; report of case with recovery following operation, *1055
Gasserian ganglion, injection of alcohol into, 214
Gastric Crises: See Tabes Dorsalis
Gastro-Intestinal Tract: See also Colon; Intestines; Stomach; etc.
new method for removal of foreign bodies from, 1347
Gellhorn, E.: Word associations as affected by deficient oxygen, excess of carbon dioxide and hyperpnea, *491
Genitals, adrenalin-like action in extracts from prostatic and related glands, 639
changes in hypophysis following lesion in infundibular sex-regulating center, 1075
Gibson, W. C.: Degeneration of *boutons terminaux* in spinal cord; experimental study, *1145
Gildea, E. F.: "Cold pressor test" in tension and anxiety; cardiochronographic study, *964
Glia: See Neuroglia
Glioma, 854
and cerebral syphilis, 1094
effect of roentgenotherapy on, *513, 879
multiple, problems of, 1079
relation of glioma of leptomeninges to neuroglia nests; report of case of astrocytoma of leptomeninges, 400
tumor of brain in monkey, 154
tumor of optic nerve, 399
Globus, J. H.: Meningiomas; origin, divergence in structure and relationship to contiguous tissues in light of phylogenesis and ontogenesis of meninges with suggestion of simplified classification of meningeal neoplasms, *667
Glueck, B.: Clinical experience with hypoglycemic therapy of psychoses, 190
Glycogen, determination in nerve tissue; carbohydrate metabolism of brain, 1071
Goldstein, K.: Psychopathology of Pick's disease, *473
Gonorrhea, encephalitis of brain stem associated with gonococcic disease, 168
Goodhart, S. P.: Presentation of case with moving-pictures, 894
Gordon, A.: Painful hemiplegia; consideration of central pain, 211
Grant, F. C.: Abscess of brain of undetermined etiology; report of 4 cases in which recovery occurred, 1124
Griffith, J. Q., Jr.: Subarachnoid hemorrhage with reference to papilledema; experimental and clinical study, 217
Griggs, D. E.: Changes in spinal cord in diabetes mellitus; report of case with autopsy, *564
Groff, R. A.: Abscess of brain of undetermined etiology; report of 4 cases in which recovery occurred, 1124
Grosh, L. C., Jr.: Observations on insulin hypoglycemic shock in treatment of psychotic patients, 438
Gross, S. W.: Case of intracranial epidermoid, 177
Growth, biologic effects of pineal extract (Hanson); accruing retardation in growth and accruing acceleration in development in successive generations of rats under continuous treatment with pineal extract, 638
biologic effects of thymus extract (Hanson), 1102
effect of liberal intakes of calcium or calcium and phosphorus on growth and body calcium, 1299
Guida, F. P.: Psychoses complicating recovery from extraction of cataract, *818
Guilt, sense of guilt and need for punishment, 1344

Hadden, S. B.: Case of isolated homonymous hemianopia, 1123
Hall, V. R.: Mode of onset of epilepsy, *744
Hallucinations, audiometric examination of patients with verbal auditory hallucinations, 161
auditory, in case of astrocytoma of left temporal lobe, 167
fantom manifestations in case of left hemiplegia, 636
joy which cures, 1089
noises in ear, tinnitus and elementary, common and verbal auditory hallucinations, 1330
visual, and lesions of visual apparatus, 418
Hamilton, S. W.: Organic syndrome in psychoses, 203
Happiness; joy which cures, 1089
Hare, C. C.: Results of roentgen treatment of tumor of pituitary gland; report on 81 patients, 48 of whom were treated exclusively by irradiation, 903
Hassin, G. B.: Changes in brain in plexectomized dogs with comments on cerebrospinal fluid, *1224
Pathologic features of multiple sclerosis and allied conditions, *713
Head: See also Cranium
congenital head-nodding (spasmus nutans) and nystagmus, 1328
gunshot wound, report of case, 906
Injuries: See also Brain, injuries
injuries, intracranial pressure in, 869
injuries; masked epilepsy and simulation of traumatic epilepsy by cerebral tumor with reference to head injuries without fracture, 872
injuries; relations between cochleovestibular system and oculomotor system in case of posttraumatic paralysis of ocular muscles, 169
Headache: See also Migraine
clinical studies in post-lumbar puncture headaches, 1322
Hearing, tests; audiometric examination of patients with verbal auditory hallucinations, 161
Heart, electrocardiography; electrocardiographic changes during encephalography, 644
rate; "cold pressor test" in tension and anxiety; cardiochronographic study, *964
rate, unsteadiness in psychotic and neurotic states, *62
Heat: See also Temperature
anatomical localization of hypothalamic center for regulation of temperature, 1073
poikilothermia with hypothalamic lesions; clinicopathologic study, *1271
Hemato-Encephalic Barrier: See Brain, blood supply; Meninges, permeability
Hematoma: See Meninges, hemorrhage
Hematoporphyrin: See under Melancholia
Hemianopia, aneurysmal dilatation of ophthalmic artery, causing superior pseudohemianopic contraction of visual field, 1092
homonymous; practical points in interpretation with report of 49 cases in which lesion in brain was verified, 881
isolated homonymous, case of, 1123
transitory word blindness associated with right homonymous hemianopia, 1328
Hemiplegia: See also Brain, hemorrhage; Paralysis
fantom manifestations in case of left hemiplegia, 636
painful: consideration of central pain, 211
vasomotor responses in hemiplegic patients, 1299
Hemophilia, paralyses associated with, 411
Hemorrhage, Subarachnoid: See Meninges, hemorrhage
Heredo-Ataxia: See under Ataxia

Herman, M.: Psychoses associated with pernicious anemia, *348
Herpes zoster, bilateral, of trigeminal nerve, 410
zoster, ophthalmic, and total paralysis of oculomotor nerve, 877
zoster ophthalmicus preceded by ocular symptoms, 1321
Heterophoria, functional disturbances of eyes, 880
Heymans, C.: Survival and revival of nerve centers following acute anemia, *304
Hindbrain: See Brain
Hinton Test: See under Syphilis
von Hippel's Disease: See Retina, tumors
Holmer, O. P.: Psychotherapy in cases of suspected organic defects in young children, 1342
Holt, W. L., Jr.: Epidemic encephalitis; follow-up study of 266 cases, *1135
Homosexuality: See Sex, perversion
Hormones: See also Endocrine Glands; Pituitary Preparations
sex, and their relation to schizophrenia, 234
sex; quantitative studies on structural changes induced in anterior hypophysis by injections of estrin, 1103
Hoskins, R. G.: Oxygen metabolism in schizophrenia, *1261
Hospital, Medical Society of St. Elizabeths Hospital, Washington, D. C., 1064
St. Elizabeths, Washington, D. C., superintendent of, 1064
Houser, G. F.: Involutional melancholia; treatment with theelin, *505
Howe, H. A.: Facial tic in relation to injury of facial nerve; experimental study, *1190
Hydrocephalus, changes in brain in plexectomized dogs with comments on spinal fluid, *1224
mechanism of internal hydrocephalus in spina bifida, 152
venous angioma of sylvian aqueduct and fourth ventricle associated with internal hydrocephalus and mental deterioration, 428
Hydrogen Ion Concentration, phosphocreatine and lactic acid changes in potassium chloride contracture of frog muscles in acid solutions, 618
Hyperpnea: See Respiration, hyperpnea
Hyperpyrexia, Artificial: See Fever
Hypertension: See Blood pressure, high
Hyperthermia: See under Fever
Hyperventilation: See Respiration, hyperpnea
Hypnosis, development of apparent unconsciousness during hypnotic reliving of traumatic experience, *1282
Hypoglycemia: See Blood sugar
Hypophysis: See Pituitary Body
Hypopituitarism: See Pituitary Body
Hypothalamus: See also Pituitary Body
anatomical localization of hypothalamic center for regulation of temperature, 1073
changes in hypophysis following lesions in infundibular sex-regulating center, 1075
conduction paths of infrathalamic region; afferent and efferent paths, 615
effects of sodium amytal and other drugs on reactivity of hypothalamus of cat, 224
histologic changes in hypothalamus, substantia nigra and inferior olive in epilepsy, 856
hypothalamic regulation of temperature in monkey, *445
myxedema, acromegaly, infundibulotuberal syndrome, melancholic delirium, oneirism, ligneous thyroiditis, pituitary adenoma and pedunculo-mesodiencephalic encephalitis, 1105
poikilothermia with hypothalamic lesions; clinicopathologic study, *1271
proposed mechanism of emotion, *725
relation to disorders of personality; report of case, *291
subthalamus and structures of subthalamomesencephalic region, 393
Icterus: See Jaundice
Idiocy: See also Feeblemindedness
mongolian; anatomic and pathologic features of mongoloidism, 404
Industrial Diseases, central nervous system in acute metallic poisoning, 855
Infantilism, Pituitary: See Pituitary Body, diseases
Infundibulum: See Hypothalamus
Ingram, W. R.: Hypothalamic regulation of temperature in monkey, *445
Insanity: See also Dementia Praecox; Depression; Melancholia; Mental Diseases
aggression and anxiety in determination and nature of manic attacks, *71
Alcoholic: See Alcoholism; Korsakoff Syndrome
delusional; constitutional aspects of paranoid reactions, 205
delusional; relation of persecutory delusions to functioning of gastro-intestinal tract, 857
delusional; religious delusions; report of case, 232
manic-depressive, anatomic-histologic studies in cases of, 853
manic-depressive; melancholia; prognostic study and case-material, 1314
mental disorder associated with child-bearing, 1312
presenile; acquired dementias, 162
venous angioma of sylvian aqueduct and fourth ventricle associated with internal hydrocephalus and mental deterioration, 428
Institute, Georgetown University Brain Research Institute, 1063
Instruments: See Apparatus
Insulin: See also Diabetes Mellitus
carbohydrate metabolism of brain; effect of varying carbohydrate and insulin supply on glycogen, free sugar, and lactic acid in mammalian brain, 617
experiences with insulin shock therapy in schizophrenia, 907
histologic changes in insulin convulsions, 856
hypoglycemic shock in treatment of psychotic patients, 438
hypoglycemic state in treatment of schizophrenia, 879
hypoglycemic treatment of psychoses, 412
response of schizophrenic subjects to hypoglycemic insulin shock, 1325
treatment of schizophrenia by production of hypoglycemic state, 880
Intelligence, behavior and personality of children with endocrine disturbances, 1339
relationship of intellect to speech defect in aphasic patients, 406
Tests: See Mental Tests
Internal Secretions: See Endocrine Glands
Intervertebral Disks: See Spine
Intestines: See also Colon; Gastro-Intestinal Tract; Stomach
pressor and oxytocic fractions of posterior pituitary extract; comparative effects on blood pressure and intestinal activity, 638
Intoxication: See Alcoholism
Iris, atrophy, relation of Argyll Robertson sign to, 1331

Jamaica-Ginger Paralysis: See Neuritis, peripheral
Jasper, H.: Studies on children with behavior problems, 1350
Jaundice, spirochetal: chronic meningitis in Weil's disease, 866
Jaws, neuralgias and ear symptoms, associated with disturbed function of temporomandibular joint, 874
Jelliffe, S. E.: Sigmund Freud as neurologist, 654
Jervis, G. A.: Phenylpyruvic oligophrenia; introductory study of 50 cases of mental deficiency associated with excretion of phenylpyruvic acid, *944
Jews, new data relative to incidence of mental disease among Jews, 156

Jolliffe, N.: Psychoses associated with pernicious anemia, *348
Jourdan, F.: Survival and revival of nerve centers following acute anemia, *304
Joy: See under Happiness
Jurisprudence, Medical; central nervous system in acute metallic poisoning, 855

Kahn, E. A.: Anterolateral chordotomy for intractable pain of tabes dorsalis, *467
Surgical treatment of pineal tumor, *833
Katz, S. E.: Psychopathology of Pick's disease, *472
Kelman, H.: Combined system disease in tabes dorsalis, *43
Kennedy, F.: Samuel Alexander Kinnier Wilson, 388
Keratitis, herpes zoster ophthalmicus preceded by ocular symptoms, 1321
Keschner, M.: Unusual case of myoclonic epilepsy, 896
Kessler, M. M.: Ayala index; preliminary report, 437
King, L. S.: Method for rapid impregnation of microglia and oligodendroglia in material fixed in formaldehyde, *362
Klingmann, T.: Art as means of expression in some of major psychoses as applied in occupational therapy, 234
Környey, S.: Michel von Lenhossék, 140
Korsakoff Syndrome, psychopathologic features of amnesic syndrome (confabulations of patients with Korsakoff's psychosis), 863
Kraines, S. H.: Word associations as affected by deficient oxygen, excess of carbon dioxide and hyperpnea, *491
Kyphosis: See Spine, curvature

Labyrinth: See Ear, internal; Equilibrium
Lamina Terminalis: See under Brain
Landry Syndrome: See Paralysis, acute ascending
Language, development of language function in children, 1340
psychology of prison language, 1081
relation of handedness to language mechanism, 405
Larsell, O.: Cerebellum; review and interpretation, *580
Lashley, K. S.: Functional determinants of cerebral localization, *371
Lateral Sinus, cranial venous sinuses; correlation between skull markings and roentgenograms of occipital bone, 647
Laubach, C. A.: New method for removal of foreign bodies from gastro-intestinal tract, 347
Laughter, appearance of spasmodic laughing in 2 cases of disseminated sclerosis, 170
"it is to laugh," 661
Laurence-Biedl Syndrome, observation of new syndrome (Biemond) resembling Laurence-Moon-Bardet syndrome, 1106
Leavitt, F. H.: "It is to laugh," 661
Left and Right-Handedness, relation of handedness to language mechanism, 405
Lemmoblastosis: See Neuritis, interstitial
Leptomeninges: See Meninges
Leptomeningitis: See under Meningitis
Levine, M.: Sympathectomy in man; its effect on electrical resistance of skin, *756
Levy, N. A.: Necrotizing encephalitis simulating tumor of brain clinically and due to necrotizing angiitis; clinicopathologic report, *775
Lewis, N. D. C.: Constitutional aspects of paranoid reactions, 205
William Alanson White, 608
Lewy, F. H.: Problem of neuritis, 222
Liber, A. F.: Case of non-neoplastic syringomyelia with Rosenthal fibers; consideration of pathogenesis of syringomyelia, 177
Lichtenstein, B. W.: Cystic tumor of third ventricle containing colloid material, *268
Lindau's Disease: See Angioma
Lipase in Blood: See Blood, lipase
Lipoma, extramedullary pial lipomas along posterior roots, 855
of brain and spinal cord, 624
Lisa, J. R.: Case of non-neoplastic syringomyelia with Rosenthal fibers; consideration of pathogenesis of syringomyelia, 177
Liver, circulation in liver on stimulation of splanchnic nerve, 1075
Lobectomy: See Brain, surgery
Locomotion: See also Movements
cortical area concerned with coordinated walking in rat, 844
Löwenberg, K.: Clinicopathologic study of astrocytomas, *1208
Lorand, S.: Judicious selection of patients for psychoanalytic therapy, 183
Lumbar Puncture: See Spinal Puncture
Lymphadenoma: See Lymphogranuloma
Lymphocytes in Meningitis: See Meningitis
Lymphogranuloma, spinal symptoms with lymphadenoma, 620

McManamy, M. C.: Involutional melancholia; treatment with theelin, *505
Macula Lutea, bilateral representation in, 1332
Mahon, G. S.: Stain for myelin sheaths in tissues embedded in paraffin, *103
Malamud, N.: Encephalomyelitis complicating measles, *1025
Lissauer's dementia paralytica; study of its pathogenesis, *27
Malaria, Therapeutic: See under Dementia Paralytica; Poliomyelitis; Syphilis
Mania: See Insanity
Marriage, marital status in relation to prevalence of mental disease, 157
personality characteristics of happily married, unhappily married and divorced persons, 1087
relation between insanity and marital condition, 626
Masserman, J.: Effects of sodium amytal and other drugs on reactivity of hypothalamus of cat, 224
Mastoid, surgical repair of facial nerve, 409
Mathematics, congenital arithmetic disability and acalculia (Henschen), 634
Matthews, R. A.: Chronic encephalitis; symptomatic treatment with benzedrine sulfate, 892
Measles complicating encephalomyelitis, *1025
German: See Rubella
Mecholyl: See Choline and Choline Derivatives
Medulla Oblongata, anatomic problem of palatal myoclonus, 168
arterial supply of lateral parolivary area of medulla oblongata in man, *1243
olivocerebellar atrophy, 1305
presence of colloid inclusions in ganglion cells of human medulla oblongata, 846
role of bulbar olives, 397
secondary vestibular fibers and medial longitudinal bundle, 660
Melancholia: See also Insanity
depressive psychoses occurring at menopause, 1315
hematoporphyrin treatment of melancholia and endogenous depressions, 412
involutional; treatment with theelin, *505
Melanin, pigmentation; relation of nerves to chromatophore pulsations, 618
Melanoblastoma, extensive pigmented nevus associated with primary melanoblastosis of leptomeninges of brain and spinal cord, 852
Melanosarcoma, primary, of brain, numerous pigmented nevi of skin and extensive neurofibromatosis of cutaneous nerves, 621
Meninges: See also Arachnoid; Pia Mater
carcinomatous cells in spinal fluid, 1080
effect of injections of colloidal thorium dioxide on ventricles and subarachnoid spaces, *340
extensive pigmented nevus associated with primary melanoblastosis of leptomeninges of brain and spinal cord, 852

Meninges—Continued
Hemorrhage: See also Brain, hemorrhage
hemorrhage; etiology of subdural hematoma, 401
hemorrhage; prognostic factors in spontaneous subarachnoid hemorrhage, *239
hemorrhage; role of scurvy in etiology of chronic subdural hematoma, 866
hemorrhage, subarachnoid, with reference to papilledema; experimental and clinical study, 217
membranous parts of brain, meninges and their blood vessels in Amblystoma, 844
permeability; hemato-encephalic barrier and sympathetic nervous system, 633
permeability to arsenic in cases of dementia paralytica before and after malaria therapy, 165
primary tumor of optic nerve, 400
tumors; atypical varieties of meningioma; multiple, recurrent and infiltrating tumors, 402
tumors; meningeal mesenchymoma of foreign body origin, 623
tumors; meningiomas; origin, divergence in structure and relationship to contiguous tissues in light of phylogenesis and ontogenesis of meninges with suggestion of simplified classification of meningeal neoplasms, *667
tumors; relation of glioma of leptomeninges to neuroglia nests; report of case of astrocytoma of leptomeninges, 400
tumors; unilateral exophthalmos produced by meningioma of middle cranial fossa, 405
Meningioma, atypical varieties of; multiple, recurrent and infiltrating tumors, 402
origin, divergence in structure and relationship to contiguous tissues in light of phylogenesis and ontogenesis of meninges with suggestion of simplified classification of meningeal neoplasms, *667
unilateral exophthalmos produced by meningioma of middle cranial fossa, 405
Meningitis: See also Arachnoid; Meningococci; Meningo-Encephalitis
acute cystic pneumococcic meningitis in patient with dementia paralytica, 401
acute idiopathic or epidemic serous meningitis, 867
acute lymphocytic, 1092
chronic, in Weil's disease, 866
due to Brucella in child, 1091
epidemic in mouse colony due to virus of acute lymphocytic choriomeningitis, 633
lymphocytic, virus etiology of 1 form of, 866
meningeal reaction in erythema nodosum, 868
otitic; report of case in which treatment with continuous spinal drainage was used, 632
pathologic histology of lymphocytic choriomeningitis in monkeys, 633
Serosa Circumscripta Spinalis: See under Arachnoid
surgical treatment of meningitis of otitic and nasal origin, 1324
tuberculous, pathogenesis of, 1093
tuberculous, role of bovine type of bacillus in etiology in children, 867
tuberculous, significance of diminution of spinal fluid sugar in, 865
Meningococci: See also under Meningitis
ocular complications of cerebrospinal meningitis, 164
significance of serologic types among meningococci, 865
Meningo-Encephalitis, 231. See also Encephalitis; Meningitis
epidemic lymphocytic; report of 37 cases occurring in Philadelphia, 1090
tumor syndrome with hyperthermia and visceral disorders due to chronic basilar tuberculous meningo-encephalitis, 166
Menopause, depressive psychoses occurring at, 1315
Mental Deficiency: See Feeblemindedness
Mental Diseases: See also Children; Dementia Praecox; Feeblemindedness; Insanity; Mental Hygiene; Neuroses; Psychoses; etc.
anatomic and clinical study of case of Friedreich's disease associated with mental disturbances, 1079
art as means of expression in some of major psychoses as applied in occupational therapy, 234
constitutional relationship between tuberculosis and mental disease, 630
disease process resembling amyotrophic lateral sclerosis with mental symptoms, 407
effect of hypertonic solution of dextrose in cases of acute confusion and agitation, 1327
fate of 150 psychiatric outpatients, 1313
fugue reaction during course of cataphrenic episode, 163
homonymous states in pernicious anemia, 1315
hypoglycemic treatment of psychoses, 412
marital status in relation to prevalence of, 157
mental syndrome of corpus callosum tumors, 870
mood—content problem and thymonoic reactions, *90
new data relative to incidence among Jews, 156
organic syndrome in psychoses, 203
problem of symptomatic psychoses, 628
psychopathology of Pick's disease, *473
psychoses associated with pernicious anemia, *348
relation between insanity and marital condition, 626
selective involvement of layers of cerebral cortex in, 1306
significance of sedimentation rate in neurology and psychiatry, 645
subcortical prefrontal lobotomy in treatment of certain psychoses, 225
sugar in blood and spinal fluid, 173
unsteadiness of heart rate in psychotic and neurotic states, *62
Mental Hygiene, student mental-hygiene work at University of Michigan, 4 years of, 156
utilization of play in construction of healthy mental attitudes, 1083
Mental Tests: See also Character; Personality
word associations as affected by deficient oxygen, excess of carbon dioxide and hyperpnea, *491
Mesencephalon: See under Brain
Mesenchymoma, meningeal, of foreign body origin, 623
Metals, Poisoning: See under Poisons and Poisoning
Microcephaly, congenital malformation of cerebrum associated with microcephaly, 152
Microglia: See Neuroglia
Midbrain: See Brain
Migraine, effect of ergotamine tartrate on pressure of spinal fluid and blood during migraine headache, 172
Milhorat, A. T.: Studies in diseases of muscle; metabolism of creatine and creatinine in progressive muscular dystrophy, *992
Milk, role of bovine type of bacillus in etiology of tuberculous meningitis in children fed on raw milk, 867
Mind Blindness: See Blindness, psychic
Minor Syndrome: See Spinal Cord, injuries
Mitchell, R. S.: Prostigmin in diagnosis and treatment of myasthenia gravis, 1349
Molitch, M.: Behavior, personality and intelligence of children with endocrine disturbances, 1339
Mongolism: See Idiocy, mongolian
Monsters, microcephalic fetus without eyes and nose and with serious defects of forebrain, cerebellum, inner ear and endocrine glands, 846
Morphine, statistical study of 90 addicts, 631
Morter, R. A.: "Sex hormones" and their relation to schizophrenia, 234

Most, H.: Psychoses associated with pernicious anemia, *348
Movements: See also Automatism; Eyes, movements; Locomotion; Muscles
akinetic states following introduction of air into third ventricle and their significance, 175
congenital motor disturbances of cranial nerves in 1 family, 11 cases, 876
dyskinesia, presentation of case with moving-pictures, 894
dyskinesia; presentation of cases, 895
specific responses elicitable from subdivisions of motor cortex of cerebrum of cat, 614
Muncie, W.: Mood—content problem and thymonoic reactions, *90
Muscles, chemical changes in hypophysectomized toad, 637
chemical transmission of excitation from motor nerve to voluntary muscle, 849
cholesterol content of, 847
Dystrophy: See Dystrophy, muscular
effects of drugs on transmission from nerve to voluntary muscle and accommodation to different rates of destruction of chemical transmitter, 849
hypertrophy and muscle cramps in case of polyradiculitis, 1321
influence of high pressure on action currents of muscle and nerve, 620
innervation of muscle of accommodation in eye of teleost, Holocentrus, 1066
myographic and electromyographic studies of myasthenia gravis, 413
Ocular: See under Eyes
phosphocreatine and lactic acid changes in potassium chloride contracture of frog muscles in acid solutions, 618
physiologic function of orbicularis palpebrarum muscle and problem of superior portion of facial nerve, 393
studies in diseases of; metabolism of creatine and creatinine in progressive muscular dystrophy, *992
Myasthenia gravis, myographic and electromyographic studies of, 413
gravis, prostigmin in diagnosis and treatment of, 1349
gravis, prostigmin treatment for, 1327
gravis, treatment of; report of 6 cases, 423
gravis, use of prostigmin as diagnostic test of, 890
Myelin: See under Nervous System
Myelitis: See Encephalomyelitis
Myelography: See Spinal Canal Roentgenography
Myelomalacia: See Spinal Cord
Myelopathy: See Spinal Cord
Myers, H. B.: Experimental studies of serum lipase in multiple sclerosis, *288
Myoclonus, palatal, anatomic problem of, 168
Myopia, obesity and ocular symptoms in mentally alert children due to hypothyroidism, 637

Narcolepsy: See Sleep, disturbances
Narcosis: See Anesthesia
Nasopharynx, unilateral global paralytic syndrome of 12 cranial nerves, 170
Necrosis, necrotizing encephalitis simulating tumor of brain clinically and due to necrotizing angiitis; clinicopathologic report, *775
Nerves: See also under Neuralgia; Neuritis; Paralysis
Cells: See Neurons
changes in lateral-line organs during life of newt, Triturus viridescens, 845
cochlear, reaction to destruction of its end organs; study on deaf albino cats, 613
congenital motor disturbances of cranial nerves in 1 family, 11 cases, 876
facial; physiologic function of orbicularis palpebrarum muscle and problem of superior portion of facial nerve, 393
facial tic in relation to injury of facial nerve; experimental study, *1190
Nerves—Continued
influence of high pressure on action currents of muscle and nerve, 620
intramedullary course of dorsal root fibers of each of first 4 cervical nerves, 1065
isolated electric stimulation of 2 vestibular nerves; double chronaxia on each side, 883
limb movements studied by electrical stimulation of nerve roots and trunks in Amblystoma, 612
olfactory; change in volume of olfactory and accessory olfactory bulbs of albino rat during postnatal life, 612
Optic: See also Neuritis, optic
optic connections of diencephalon and midbrain of cat, 391
optic; differential oxygen uptake of regions of Limulus optic nerve as related to distance from sense organ, 143
optic, primary tumors of, 400, 405
optic, tumor of, 399
peripheral, neurofibroma and neurofibrosarcoma unassociated with Recklinghausen's disease; report of 25 cases, 874
relation to chromatophore pulsations, 618
roots; extramedullary pial lipomas along posterior roots, 855
roots; muscular hypertrophy and muscle cramps in case of polyradiculitis, 1321
roots; polyradiculoganglionitis of Landry's type in syphilitic patient, 1321
Spinal: See also Nerves, roots
spinal, growth responses to grafted brain tissue, 1296
splanchnic, circulation in liver on stimulation of, 1075
splanchnic, is resection justified in treatment of permanent essential arterial hypertension? 1326
survival and revival of nerve centers following acute anemia, *304
Trigeminal: See also Neuralgia, trigeminal
trigeminal, bilateral herpes zoster of, 410
Vagus: See also under Heart
vagus; morphology of neurons migrated from ganglion nodosum of vagus in birds, 1295
Nervous System: See also Brain; Cerebellum; Nerves; Reflex; Spinal Cord; etc.
action potentials in crayfish; temporal relations in presynaptic and postsynaptic responses, 1071
adaptation of original Weigert technic for staining myelin sheaths in formaldehyde-pyroxylin material, *1291
autonomic, action of yohimbine on, 1303
autonomic, relationship to pathogenesis of epilepsy, *16
carcinomatous cells in spinal fluid, 1080
central, in acute metallic poisoning, 855
changes in cells of striated ducts of cat's submaxillary gland after autonomic stimulation and nerve section, 1070
diffuse lemmoblastosis of central nervous system, 1308
Diseases: See also Epilepsy; Mental Diseases; Neuritis; Neuroses; Psychoses; etc.
diseases; combined system disease in tabes dorsalis, *43
distant effects of high frequency currents on nerves, 150
distribution of sympathetic nerve fibers to hind limb of cat, 843
embryology in grasshopper, Melanoplus differentialis (Acrididae; Orthoptera), 1067
epileptiform convulsions from "remote" excitation, *259
influence of sympathetic nerve fibers on coronary vessels, 1075
physiologic effects of acteyl-beta-methylcholine (mecholyl) and its relationship to other drugs affecting autonomic nervous system, 1298
physiology; effect of lesions in central nervous system of rat upon reflex time, 144
relationship of microglia cells to blood vessels, 1069

Nervous System—Continued
role of hypophysis in transmission of irritation, 1107
significance of sedimentation rate in neurology and psychiatry, 645
spinal fluid in vascular diseases of central nervous system, 641
stain for myelin sheaths in tissues embedded in paraffin, *103
sugar in blood and spinal fluid, 173
Surgery: See Sympathectomy
sympathetic, and hemato-encephalic barrier, 633
Syphilis: See Syphilis
tumors; dermoid and epidermoid tumors (cholesteatomas) of central nervous system, 870
tumors; lipomas of brain and spinal cord, 624
vegetative disturbances following encephalography, 175
vegetative, in dementia praecox, 640
Neuralgia and ear symptoms, associated with disturbed function of temporomandibular joint, 874
glossopharyngeal, 876
trigeminal, occurrence in patients having multiple sclerosis, 634
Neuritis, interstitial; diffuse lemmoblastosis of central nervous system, 1308
interstitial; progressive familial hypertrophic neuritis (Dejerine-Sottas), 410
multiple; etiology of polyneuritis in alcohol addict, 875
multiple; gastrogenous polyneuritis, 876
multiple; relation of spinal fluid to polyneuritis, 174
neuritic manifestations in diabetes mellitus, 408
optic, of dental origin, 420
optic; subarachnoid hemorrhage with reference to papilledema; experimental and clinical study, 217
peripheral; follow-up study of 35 cases of paralysis caused by adulterated Jamaica-ginger extract, 1320
problem of, 222
Neurofibroma and neurofibrosarcoma of peripheral nerves unassociated with Recklinghausen's disease; report of 25 cases, 874
Neurofibromatosis, familial congenital Bourneville's disease (tuberous sclerosis) associated with symptoms of neurofibromatosis (Recklinghausen's disease), 635
primary melanosarcoma of brain, numerous pigmented nevi of skin and extensive neurofibromatosis of cutaneous nerves, 621
Neurofibrosarcoma and neurofibroma of peripheral nerves unassociated with Recklinghausen's disease; report of 25 cases, 874
Neuroglia, method for rapid impregnation of microglia and oligodendroglia in material fixed in formaldehyde, *362
relation of glioma of leptomeninges to neuroglia nests; report of case of astrocytoma of leptomeninges, 400
relationship of microglia cells to blood vessels, 1069
Neurology, progress in 1934, 870
Sigmund Freud as neurologist, 654
Neuromyelitis Optica: See Neuritis, optic
Neurons, autonomic, Nissl granules of, 613
degeneration of *boutons terminaux* in spinal cord; experimental study, *1145
electrical excitability of motoneurons, 143
morphology of neurons migrated from ganglion nodosum of vagus in birds, 1295
results of recent studies in field of neuron theory, 850
Neuropsychiatry, residencies in, 1064
Neuroses: See also Mental Diseases; Psychoses; etc.
problem of long-continued, low grade fever, 857
psychogenic aspects of skin diseases, 858
social neurosis, 1112
Neurosurgery: See Sympathectomy
Neurosyphilis: See Syphilis
Nevi, extensive pigmented nevus associated with primary melanoblastosis of leptomeninges of brain and spinal cord, 852
primary melanosarcoma of brain, numerous pigmented nevi of skin and extensive neurofibromatosis of cutaneous nerves, 621
Newell, R. R.: Device for controlled faradic stimulation, *1289
Nielsen, J. M.: Unilateral cerebral dominance as related to mind blindness; minimal lesion capable of causing visual agnosia for objects, *108
Nissl Granules: See Neurons
Nitrogen and sulfur metabolism in suprarenalectomized rats, 638
effect of injection of certain nitrogen-containing compounds into cisterna magna on blood pressure of dogs, 1322
Nowak, S. J. G.: Survival and revival of nerve centers following acute anemia, *304
Nucleus Pulposus: See Spine, intervertebral disks
Nunberg, H.: Psychologic interrelation of physician and patient, 1109
Nystagmus: See also Cerebellum; Ear, internal; Equilibrium; Reflex, aural
and congenital head-nodding, 1328

Oberndorf, C. P.: Dictaphonic reproduction in case of depersonalization, 429
Feeling of stupidity, 1111
Obesity and ocular symptoms in mentally alert children due to hypothyroidism, 637
hyperostosis frontalis interna, 1094

Obituaries:

von Lenhossék, Michel, 140
Stearns, William G., 1122
White, William Alanson, 608
Wilson, Samuel Alexander Kinnier, 388

Occipital Bone, cranial venous sinuses; correlation between skull markings and roentgenograms of occipital bone, 647
Occupational therapy, art as means of expression in some of major psychoses as applied in, 234
Oil, prevention of nutritional encephalomalacia in chicks by vegetable oils and their fractions, 1076
Old Age, endocrine glands and brain in, 640
senile erotism in women, 1089
Oldberg, E.: Changes in brain in plexectomized dogs with comments on cerebrospinal fluid, *1224
Scoliosis with tumor of spinal cord, 1119
Olfactometry: See under Smell
Olfactory Bulb: See Nerves, olfactory
Glands: See under Smell
Oligodendroglia: See Neuroglia
Oligophrenia: See Feeblemindedness
Olivary Bodies: See Medulla Oblongata
Olsen, C. W.: Changes in spinal cord in diabetes mellitus; report of case with autopsy, *564
Ophthalmoplegia: See Eyes, paralysis
Optic Chiasm, iodoventriculographic picture of chiasmatic arachnoiditis, 1334
traumatic lesions of, 1329
Optic Disk, Choked: See Neuritis, optic
Optic Thalamus: See Thalamus
Orbit, multiple orbitocranial lesions from lead shot; syndrome of hemorrhage of cavernous sinus, 165
Orloff, M. E.: Role of wish-fulfilling mechanism in psychosis, 1345
Orzechowski, K.: Relationship of autonomic nervous system to pathogenesis of epilepsy, *16
Osteomyelitis of frontal bone; notes on 3 cases, 1091
Otitis Media, otitic meningitis; report of case in which treatment with continuous spinal drainage was used, 632
surgical treatment of meningitis of otitic and nasal origin, 1324

Otolith Apparatus, chemical analysis of otoliths and endolymphatic sac deposits in Amblystoma tigrinum, 612
Ovary, relationship of anterior pituitary gland to thyroid and ovary, 1103
Oxidation, metal catalysts in biologic oxidations; tissue inhibitors, 396
Oxygen, deficiency; relationship between alcoholic intoxication and anoxemia, 847
deficiency; word associations as affected by deficient oxygen, excess of carbon dioxide and hyperpnea, *491
differential oxygen uptake of regions of Limulus optic nerve as related to distance from sense organ, 143
metabolism in schizophrenia, *1261

Pain: See also Sensation and Sensations
anterolateral chordotomy for intractable pain of tabes dorsalis, *467
occurrence of trigeminal neuralgia in patients having multiple sclerosis, 634
painful hemiplegia; consideration of central pain, 211
Palate, anatomic problem of palatal myoclonus, 168
Palsy: See Paralysis
Papez, J. W.: Connections between striatum and substantia nigra in human brain, *550
Proposed mechanism of emotion, *725
Papilledema: See Neuritis, optic
Paralysis: See also Eyes, paralysis; Hemiplegia; Poliomyelitis
acute ascending; Landry's paralysis, 2 anatomoclinical observations of, 1101
acute ascending; polyradiculoganglionitis of Landry's type in syphilitic patient, 1321
associated with hemophilia, 411
Bell's: See Paralysis, facial
facial; clinical and electrical study of case of partial hereditary and familial facial diplegia, 1320
facial; surgical repair of facial nerve, 409
flaccid, mechanism in cerebral hemiplegia, 398
General: See Dementia Paralytica
Infantile: See Poliomyelitis
ophthalmic herpes zoster and total paralysis of oculomotor nerve, 877
progressive, of dorsal interosseous nerve, 885
unilateral global paralytic syndrome of 12 cranial nerves, 170
Paranoia: See Insanity, delusional
Paresis: See Dementia Paralytica
Parietal Lobe: See Brain
Parkinsonism: See also Encephalitis
tuberculous encephalitis of striatum associated with parkinsonian syndrome, 867
Patterson, R. M.: Encephalographic findings in dementia praecox, 439
Peptic Ulcer, ulceration in digestive tract of dog following intracranial procedures, 395
Perivasculitis: See Brain, blood supply
Personality, behavior and intelligence of children with endocrine disturbances, 1339
characteristics of happily married, unhappily married and divorced persons, 1087
dictaphonic reproduction in case of depersonalization, 429
relation of hypothalamus to disorders of personality; report of case, *291
significance of Rorschach test, 860
Phobia: See Anxiety
Phosphates in Blood: See Blood, phosphates
Phospholipids: See Blood, fats and lipoids
Phosphorus, effect of liberal intakes of calcium or calcium and phosphorus on growth and body calcium, 1299
Physician, psychologic interrelation of physician and patient, 1109
Physostigmine, chemical transmission of excitation from motor nerve to voluntary muscle, 849
Pia Mater: See also Meninges
cerebral circulation; effect of alcohol on cerebral vessels, *321
extramedullary pial lipomas along posterior roots, 855
Pick's Disease: See Brain, atrophy
Pineal Gland, biologic effects of pineal extract (Hanson); accruing retardation in growth and accruing acceleration in development in successive generations of rats under continuous treatment with pineal extract, 638
roentgenologic study of orientation of pineal body; comparison of proportional and graphic method in absence of tumor of brain, *1199
tumor, operative experience in cases of, 878
tumor, surgical treatment of, *833
Pituitary Body: See also Hypothalamus; Sella Turcica
change in basophil cells of pituitary gland in common to conditions which exhibit syndrome attributed to basophil adenoma, 1104
changes in hypophysis following lesion in infundibular sex-regulating center, 1075
chemical changes in muscle of hypophysectomized toad, 637
cytological changes in hypophysis cerebri of garter snake (Thamnophis radix) following thyroidectomy, 393
diseases; hypophysial infantilism; treatment with anterior hypophysial extract, 637
diseases; report of case of "Simmond's disease" with recovery, 639
diseases; treatment of pituitary infantilism with anterior pituitary extract, 1324
endocrine factor in pathogenesis of arterial hypertension, increased intracranial pressure, and premature arteriosclerosis; role of hypophysis, 1106
interrelationships among urinary, pituitary and placental gonadotropic factors, 1104
is all colloid observed in midbrain of hypophysial origin? 1297
pars nervosa of hypophysis, 1120
pituitary-hypothalamic mechanism; experimental occlusion of pituitary stalk, 1072
quantitative studies on structural changes induced in anterior hypophysis by injections of estrin, 1103
relation of basophilic cells of neurohypophysis to hypertension and eclampsia, 1108
relationship of anterior pituitary gland to thyroid and ovary, 1103
responses of normal and hypophysectomized rabbits to adrenalin, 1105
role of hypophysis in transmission of irritation, 1107
significance of different types of cells of anterior pituitary, 1070
tumors, results of roentgen treatment; report on 81 patients, 48 of whom were treated exclusively by irradiation, 903
tumors; treatment of intrasellar tumors by radon, 879
Pituitary Preparations, effect of pituitary (posterior lobe) extract upon urinary flow, 1105
pressor and oxytocic fractions of posterior pituitary extract; comparative effects on blood pressure and intestinal activity, 638
Placenta, interrelationships among urinary, pituitary and placental gonadotropic factors, 1104
Play, primal scene and destiny, 626
utilization in construction of healthy mental attitudes, 1083
Plexectomy: See Choroid Plexus
Plexus: See Choroid Plexus
Pneumography: See Brain, roentgenography
Poisons and Poisoning: See also under names of various substances, as Chenopodium; etc.
central nervous system in acute metallic poisoning, 855
hemorrhages into floor of fourth ventricle in intoxications and inflammations of brain, 1308

Polioencephalitis: See Encephalitis
Polioencephalomyelitis: See Encephalomyelitis
Poliomyelitis: See also Encephalomyelitis
epidemic, malariotherapy after acute paralytic stage in, 1327
experimental, contribution to pathologic picture in, 1081
poliomyelopathia chronica; report of case with histologic study, *537
Pollock, L. J.: Carbohydrate metabolism in epilepsy, 229
Polyneuritis: See Korsakoff Syndrome; Neuritis, multiple
Pons Varolii, anatomic problem of palatal myoclonus, 168
Poriomania: See Automatism
Porphyrin in Urine: See Urine, porphyrin
Position: See Posture
Posture: See also under Reflex
factors producing lumbar spinal fluid pressure in man in erect posture, *1158
nucleus of posterior longitudinal bundle, fibers arising therefrom and probable relation of both to automatic posture of head, 1297
position of feet in station of man; relations of these phenomena to state of vestibular apparatus, 150
Potassium chloride, phosphocreatine and lactic acid changes in potassium chloride contracture of frog muscles in acid solutions, 618
Pregnancy: See also Puerperium; etc.
influence of pituitary-like substance in human pregnancy urine on motor components of sexual behavior in South African clawed toad (Xenopus laevis), 147
urine in; interrelationships among urinary, pituitary and placental gonadotropic factors, 1104
Pressure, high, influence on action currents of muscle and nerve, 620
Preu, P. W.: Psychoses complicating recovery from extraction of cataract, *818
Pringle's Disease: See Sclerosis, tuberous
Prostate, adrenalin-like action in extracts from prostatic and related glands, 639
cancer; transitory word blindness associated with right homonymous hemianopia in patient with cancer of prostate, 1328
Prostigmin, depressant peripheral effect of prostigmin and its temporary antagonism by curarine, 1300
Therapy: See Myasthenia gravis
Protein, quantities lost by various organs and tissues of body during fast, 847
Psychoanalysis: See also Psychotherapy
feeling of stupidity, 1111
final goal of psychoanalytic treatment, 1313
importance of dream-analysis for psychological development, 860
introjection and schizophrenia, 157
judicious selection of patients for psychoanalytic therapy, 183
logic of emotions and its dynamic background, 159
primal scene, play and destiny, 626
projection, 1311
psychologic interrelation of physician and patient, 1109
purposive accidents as expression of self-destructive tendencies, 160
role of wish-fulfilling mechanism in psychosis, 1345
sense of guilt and need for punishment, 1344
sociological significance of communism considered in light of, 1085
transference phenomenon in case of phobia, 1116
Psychoneuroses: See Neuroses; Psychoses
Psychoses: See also Insanity; Mental Diseases; Neuroses; etc.
bromide psychosis, study of 50 cases, 653
clinical experience with hypoglycemic therapy of, 190
complicating recovery from extraction of cataract, *818
evaluation of biochemical approach to, 207
Psychoses—Continued
hypoglycemic treatment; experiences at Bellevue Hospital, 191
insulin hypoglycemic shock in treatment of psychotic patients, 438
lesions of corpus callosum among psychotic persons, 1347
new method of treatment for acute postoperative and posttraumatic psychoses, 1336
origin and nature of hypoglycemic therapy of, 188
possibilities of surgical treatment in treatment for certain psychoses; first trial of psychosurgery; technic and results, 1089
role of wish-fulfilling mechanism in, 1345
symptomatic, with bromide intoxication, 1084
Psychotherapy: See also Psychoanalysis
in cases of suspected organic defects in young children, 1342
Puerperium, mental disorder associated with child-bearing, 1312
Pulse, rate; "cold pressor test" in tension and anxiety; cardiochronographic study, *964
Punishment, sense of guilt and need for punishment, 1344
Pupils, Argyll Robertson sign, 1331
central path of light reflex, 843
isolated abolition of light reflex (etiologic value of Argyll Robertson sign); nonsyphilitic form, 418
Putnam, T. J.: Adaptation of original Weigert technic for staining myelin sheaths in formaldehyde-pyroxylin material, *1291
Disseminated encephalomyelitis; histologic syndrome association with thrombosis of small cerebral vessels, 1127
Vascular architecture of lesions of multiple sclerosis, *1
Pyknolepsy, 634
Pyramidal Tract, dissociation of cortical excitation from cortical inhibition by pyramid section and syndrome of that lesion in cat, 144

Radiations: See also Roentgen Rays
consideration of biological factors influencing radiosensitivity of cells, 617
Radiculitis: See Nerves, roots
Ranson, S. W.: Hypothalamic regulation of temperature in monkey, *445
Rathmell, T. K.: Lesions of corpus callosum among psychotic persons, 1347
Read, C. F.: Meningo-encephalitis, 231
Reading, development of language function in children, 1340
Recklinghausen's Disease: See Neurofibromatosis
Reese, H. H.: Experiences with insulin shock therapy in schizophrenia, 907
Reflex: See also Automatism
aural; labyrinthine reflexes after otolithic membranes have been thrown off, 620
Carotid Sinus: See Carotid Sinus
effect of experimental lesions of cortex on "psychogalvanic reflex" in cat, *308
effect of lesions in central nervous system of rat upon reflex time, 144
posture; physiological study of cerebral motor cortex and control of posture in sloth, 143
pupillary; central path of light reflex, 843
pupillary; isolated abolition of light reflex (etiologic value of Argyll Robertson sign); nonsyphilitic form, 418
superficial abdominal, 848
tendon; clinical picture of minor cord lesions in association with injuries of cervical spine, 1318
Reider, N.: Hyperostosis frontalis interna; degenerative disease of brain, 658
Religion; religious delusions; report of case, 232
Respiration, cortical innervation of respiratory movements; slowing of respiratory movements by cerebral stimulation, 397
hyperpnea; word associations as affected by deficient oxygen, excess of carbon dioxide and hyperpnea, *491

Retina: See also Macula Lutea
cerebral representation in chimpanzee, 416
tumors; roentgenographic diagnosis of retinoblastoma, 1333
tumors; von Hippel's disease; Lindau's disease, 872, 1095
volumetric measurements of contractile elements of rods and cones, 614
Retinoblastoma, roentgenographic diagnosis of, 1333
Reye, H. A.: Religious delusions; report of case, 232
Richter, C. P.: Sympathectomy in man; its effect on electrical resistance of skin, *756
Richter, H.: Unsteadiness of heart rate in psychotic and neurotic states, *62
Roback, H. N.: Myelomalacia without thrombosis following indirect trauma (strain), 658
Roentgen Rays: See also Radiations
effect of roentgenotherapy on gliomas, *513
late injury of human brain resulting from roentgen irradiation, 154
Rorschach Test: See Personality
Rosenheck, C.: Venous angioma of sylvian aqueduct and fourth ventricle associated with internal hydrocephalus and mental deterioration, 428
Rubella, encephalitis following German measles, 650
Rundles, R. W.: Connections between striatum and substantia nigra in human brain, *550

Sager, O.: Sensory functions of optic thalamus of monkey (Macacus rhesus); symptomatology and functional localization investigated with method of local strychninization, *913
Sakel, M.: Origin and nature of hypoglycemic therapy of psychoses, 188
Sands, I. J.: Unusual case of intracranial aneurysm; clinical and pathologic demonstration, 649
Sarcoma: See Melanosarcoma; Neurofibrosarcoma; etc.
Savitsky, N.: Ayala index; preliminary report, 437
Schele, H.: Use of prostigmin as diagnostic test of myasthenia gravis, 890
Schilder, P.: Social neurosis, 1112
Schilder-Flatau's Disease: See Encephalitis periaxialis diffusa
Schizophrenia: See Dementia Praecox
Schube, P. G.: Involutional melancholia; treatment with theelin, *505
Schwab, D. M.: Adaptation of original Weigert technic for staining myelin sheaths in formaldehyde-pyroxylin material, *1291
Schwab, R. S.: Prostigmin in diagnosis and treatment of myasthenia gravis, 1349
Schwartz, H. G.: Effect of experimental lesions of cortex on "psychogalvanic reflex" in cat, *308
Schwarz, G.: Fracture dislocation in region of atlas and axis with consideration of delayed neurologic manifestations and roentgenographic features, 426
Sciatica, air myelography in diagnosis of lesions of spinal canal with reference to those of nucleus pulposus and to "sciatic syndrome," 1126
Sclerosis: See also Arteriosclerosis
bilateral atrophic lobar sclerosis following thrombosis of superior longitudinal sinus, 1078
combined, liver therapy for, 878
diffuse cerebral sclerosis, study of, 853
diffuse, of cerebellum, 622
disease process resembling amyotrophic lateral sclerosis with mental symptoms, 407
disseminated, appearance of spasmodic laughing in 2 cases of, 170
multiple, and allied conditions, pathologic features, *713
Sclerosis—Continued
multiple; atrophy of parietal and cerebellar lobes associated in certain cases with multiple sclerosis, 218
multiple, experimental studies of serum lipase in, *288
multiple; occurrence of epidemic encephalitis combined with multiple sclerosis, 621
multiple; occurrence of trigeminal neuralgia in patients having multiple sclerosis, 634
multiple; relation between disseminated nonsuppurative encephalomyelitis and multiple sclerosis, 624
multiple, vascular architecture of lesions of, *1
tuberous; familial congenital Bourneville's disease associated with symptoms of neurofibromatosis (Recklinghausen's disease), 635
Scoliosis: See Spine, curvature
Scott, E.: Relation of increased intracranial tension to arterial hypertension, 886
Scott, M.: Air myelography in diagnosis of lesions of spinal canal with reference to those of nucleus pulposus and to "sciatic syndrome," 1126
Atrophy of parietal and cerebellar lobes associated in certain cases with multiple sclerosis, 218
Curve for sugar content of blood following encephalography; comparison with usual curve for dextrose tolerance, *985
Scott, W. A.: Incidence of pulmonary tuberculosis in schizophrenic patients during period of 5 years in Ypsilanti State Hospital, 440
Scurvy, role in etiology of chronic subdural hematoma, 866
Secretions, Internal: See Endocrine Glands
Sella Turcica, tumors of sellar region, 873
Semicircular Canals: See Ear, internal
Senility: See Old Age
Sensation and Sensations: See also Pain; Pressure; Smell; etc.
cortical sensory disturbances in man, 1074
inhibition and extinction of sensitive points of skin, 1302
sensory functions of optic thalamus of monkey (Macacus rhesus); symptomatology and functional localization investigated with method of local strychninization, *913
Septicemia, changes in spinal cord and posterior root ganglions in sepsis, 1102
Sex, influence of pituitary-like substance in human pregnancy urine on motor components of sexual behavior in South African clawed toad (Xenopus laevis), 147
perversion; unconscious homosexuality, 1344
senile erotism in women, 1089
Shingles: See Herpes zoster
Silverstein, A.: Progressive paralysis of dorsal interosseous nerve, 885
Simmonds' Disease: See Pituitary Body, diseases
Sinus, Thrombosis: See under Thrombosis
Sinuses, Nasal; surgical treatment of meningitis of otitic and nasal origin, 1324
Skin diseases, psychogenic aspects of, 858
sympathectomy in man; its effect on electrical resistance of skin, *756
Skull: See Cranium
Sleep, disturbances; contribution to history of narcolepsy, *136
disturbances; symptomatology of narcolepsy and its treatment, 1302
prolonged, recurrent attacks of, 861
Sloan, L. H.: Association of carotid sinus reflexes with syncope and convulsions; report of 4 cases, *761
Smell, sense of; localization of tumors of frontal lobe of brain by quantitative olfactory tests, 644
summation of olfactory impulses from 2 olfactory membranes and its physiological significance, 616
Societies, Medical Society of St. Elizabeths Hospital, Washington, D. C., 1064

Society Transactions:
Boston Society of Psychiatry and Neurology, 1348
Chicago Neurological Society, 222, 658, 906, 1118
Detroit Society of Neurology and Psychiatry, 232, 438
New York Academy of Medicine, Section of Neurology and Psychiatry, 177, 648
New York Neurological Society, 428
New York Neurological Society and New York Academy of Medicine, Section of Neurology and Psychiatry, 188, 1109
New York Neurological Society and Philadelphia Neurological Society, 894
Philadelphia Neurological Society, 211, 423, 661, 885, 1123
Philadelphia Psychiatric Society, 1336

Sodium amytal, effects of sodium amytal and other drugs on reactivity of hypothalamus of cat, 224
Solomon, P.: Studies on children with behavior problems, 1350
Somnambulism, extreme encephalitic parkinsonism with contractures which relax during somnambulistic state, 166
Sottas-Dejerine's Disease: See Neuritis, interstitial
Spasm: See also Chorea; Convulsions; Epilepsy; etc.
facial tic in relation to injury of facial nerve; experimental study, *1190
histopathologic alterations in case of buccolingual spasm of postencephalitic origin, 1080
muscular hypertrophy and muscle cramps in case of polyradiculitis, 1321
Spasmus Nutans: See under Head
Speech, defects; anatomic explanation of dysarthria associated with dementia paralytica, 873
excision of speech area without resultant aphasia, 430
relationship of intellect to speech defect in aphasic patients, 406
words and masses; pictorial contribution to psychology of stammering, 1084
Spina Bifida, mechanism of internal hydrocephalus in, 152
Spinal Canal Roentgenography, air myelography in diagnosis of lesions of spinal canal with reference to those of nucleus pulposus and to "sciatic syndrome," 1126
Spinal Cord: See also Meninges; Nervous System; Pyramidal Tract; etc.
abscess of, 1319
all or none law; block; alternans, bigemini and allied phenomena as properties of spinal cord, 619
changes in cord and posterior root ganglions in sepsis, 1102
changes in diabetes mellitus; report of case with autopsy, *564
clinical picture of minor cord lesions in association with injuries of cervical spine, 1318
combined system disease in tabes dorsalis, *43
compression caused by ecchondrosis of intervertebral fibrocartilage, 1316
degeneration of *boutons terminaux* in; experimental study, *1145
differentiation of colored spinal fluids, 1322
injuries; syndrome of epiconus of Minor, 1319
medullary alterations in case of chronic alcoholism, 621
myelomalacia without thrombosis following indirect trauma (strain), 658
neoplasms; review of 42 surgical cases, 1316
poliomyelitis (poliomyelopathia) chronica; report of case with histologic study, *537
posterior column fibers and their termination in Macacus rhesus, 392
secondary vestibular fibers and medial longitudinal bundle, 660
Spinal Cord—Continued
surgery; anterolateral chordotomy for intractable pain of tabes dorsalis, *467
syphilis of, 425
tuberculoma, operative removal of, 1315
tumors; new method of treatment for acute postoperative and posttraumatic psychoses, 1336
tumors, with scoliosis, 1119
Spinal Fluid: See Cerebrospinal Fluid
Spinal Puncture: See also Cerebrospinal Fluid
clinical studies in post-lumbar puncture headaches, 1322
Spine: See also Atlas and Axis
clinical picture of minor cord lesions in association with injuries of cervical spine, 1318
curvature; scoliosis with tumor of spinal cord, 1119
fracture dislocation in region of atlas and axis with consideration of delayed neurologic manifestations and roentgenographic features, 426
intervertebral disks; air myelography in diagnosis of lesions of spinal canal, with reference to those of nucleus pulposus and to "sciatic syndrome," 1126
intervertebral disks; clinical study of herniation of nucleus pulposus, 899
spinal compression caused by ecchondrosis of intervertebral fibrocartilage, 1316
spinal symptoms with lymphadenoma, 620
Stains and Staining, adaptation of original Weigert technic for staining myelin sheaths in formaldehyde-pyroxylin material, *1291
stain for myelin sheaths in tissues embedded in paraffin, *103
Status Epilepticus: See under Epilepsy
Marmoratus: See Corpus Striatum; Thalamus
Stearns, W. G., in memoriam, 1122
Steegmann, A. T.: Poliomyelitis (poliomyelopathia) chronica; report of case with histologic study, *537
Steinberg, S.: Unconscious homosexuality, 1344
Stomach: See also Gastro-Intestinal Tract
diseases; gastrogenous polyneuritis, 876
Ulcers: See Peptic Ulcer
Stone, L.: Myelomalacia without thrombosis following indirect trauma (strain), 658
Stone, T. T.: Huntington's chorea; genealogical study, 910
Water metabolism in relation to convulsions, *798
Stookey, B.: Clinical study of herniation of nucleus pulposus, 899
Strauss, I.: Defects in visual field of 1 eye only in patients with lesion of 1 optic radiation, 652
Prognostic factors in spontaneous subarachnoid hemorrhage, *239
Strychnine, sensory functions of optic thalamus of monkey (Macacus rhesus); symptomatology and functional localization investigated with method of local strychninization, *913
Stupidity, feeling of, 1111
Subarachnoid Space: See Meninges
Submaxillary Duct, changes in cells of striated ducts of cat's submaxillary gland after autonomic stimulation and nerve secretion, 1070
Substantia Nigra: See under Brain
Subthalamus: See Hypothalamus
Sugar in Blood: See Blood sugar
in Cerebrospinal Fluid: See Cerebrospinal Fluid
Tolerance Test: See under Dextrose
Suh, T. H.: Arterial supply of lateral parolivary area of medulla oblongata in man, *1243
Suicide, purposive accidents as expression of self-destructive tendencies, 160
Sulfur and nitrogen metabolism in suprarenalectomized rats, 638
Supra-Optic Commissure: See Nerves, optic
Suprarenalectomy: See under Adrenals
Suprarenals: See Adrenals

Swan, K. C.: Experimental studies of serum lipase in multiple sclerosis, *288
Sweat Glands, innervation of, 1068
Sympathectomy in man; its effect on electrical resistance of skin, *756
Syncope, association of carotid sinus reflexes with syncope and convulsions; report of 4 cases, *761
Syphilis: See also under names of organs and regions
cerebral, and glioma, 1094
effect of artificial fever on clinical manifestations of syphilis and Treponema pallidum, 1323
exclusion of neurosyphilis by means of Hinton reaction of blood, 644
isolated abolition of light reflex (etiologic value of Argyll Robertson sign); nonsyphilitic form, 418
of nervous system in Buriat Mongolians, 1089
of spinal cord, 425
polyradiculoganglionitis of Landry's type in syphilitic patient, 1321
Syringomyelia, non-neoplastic, with Rosenthal fibers; consideration of pathogenesis, 177

Tabes Dorsalis, abnormalities of micturition due to syphilis of nervous system, 1099
anterolateral chordotomy for intractable pain of, *467
combined system disease in, *43
medical and surgical aspects of Charcot joints, 411
Tarachow, S.: Prognostic factors in spontaneous subarachnoid hemorrhage, *239
Tarlov, I. M.: Effect of roentgenotherapy on gliomas, *513
Teeth, optic neuritis of dental origin, 420
Temperature: See also Heat
hypothalamic regulation in monkey, *445
Tetanus, chronic, presentation of patient, 1118
Tetany, parathyroid, relation of serum phosphates to, 639
Thalamus, état marbré, 852
sensory functions of optic thalamus of monkey (Macacus rhesus); symptomatology and functional localization investigated with method of local strychninization, *913
Thomas, C. B.: Cerebral circulation; effect of alcohol on cerebral vessels, *321
Thorium dioxide, colloidal, effect of injections on ventricles and subarachnoid spaces, *340
Thorner, M. W.: Treatment of myasthenia gravis; report of 6 cases, 423
Thrombosis, bilateral atrophic lobar sclerosis following thrombosis of superior longitudinal sinus, 1078
disseminated encephalomyelitis; histologic syndrome associated with thrombosis of small cerebral vessels, 1127
genesis of multiple encephalomalacia and angina pectoris in foam formation, 1080
sinus; cranial venous sinuses; correlation between skull markings and roentgenograms of occipital bone, 647
sinus; variations of cranial venous sinuses in region of torcular herophili, 632
Thymus, biologic effects of thymus extract (Hanson), 1102
Thyroid, cytological changes in hypophysis cerebri of garter snake (Thamnophis radix) following thyroidectomy, 393
hypothyroidism, obesity and ocular symptoms in mentally alert children due to, 637
relationship of anterior pituitary gland to thyroid and ovary, 1103
Tic: See Spasm
Tinnitus, noises in ear, and elementary, common and verbal auditory hallucinations, 1330
Tinsley, M.: Changes in brain in plexectomized dogs with comments on cerebrospinal fluid, *1224
Tissue: See also Cells
metal catalysts in biologic oxidations; tissue inhibitors, 396
method for rapid impregnation of microglia and oligodendroglia in material fixed in formaldehyde, *362
quantities of protein lost by various organs and tissues of body during fast, 847
Staining: See also Stains and Staining
staining; stain for myelin sheaths in tissues embedded in paraffin, *103
Tobacco, acetylcholine in tobacco amblyopia, 411
Tower, S. S.: Facial tic in relation to injury of facial nerve; experimental study, *1190
Toxicomania: See under Morphine
Transference: See Psychoanalysis
Trapp, C. E.: Involutional melancholia; treatment with theelin, *505
Tryparsamide, intolerance to, 411
Tuber Cinereum: See Hypothalamus
Tuberculoma of spinal cord, operative removal, 1315
Tuberculosis, constitutional relationship between tuberculosis and mental disease, 630
pulmonary, incidence in schizophrenic patients during period of 5 years in Ypsilanti State Hospital, 440
Tumors: See also Adenoma; Angioma; Astrocytoma; Cancer; Chondroma; Epithelioma; Glioma; Lipoma; Meningioma; etc.; and under names of organs and regions, i.e., Brain, tumors; Corpus Callosum; Cranium; Meninges; Pituitary Body; Retina; Spinal Cord; etc.
case of 3 neoplasms, 1304
dermoid and epidermoid (cholesteatomas) of central nervous system, 870
Turner, O. A.: Neuro-epithelial cyst of third ventricle; report of case with recovery following operation, *1055
Twins, hereditary factor in epilepsy, 171

Unconsciousness, apparent, development during hypnotic reliving of traumatic experience, *1282
Undulant fever, meningitis due to Brucella in child, 1091
Universities, four years of student mental-hygiene work at University of Michigan, 156
Unverricht's Disease: See under Epilepsy
Urination, effect of pituitary (posterior lobe) extract upon urinary flow, 1105
Urine, creatine; metabolism of glycolic acid in progressive muscular dystrophy, 413
phenylpyruvic acid; phenylpyruvic oligophrenia; introductory study of 50 cases of mental deficiency associated with excretion of phenylpyruvic acid, *944
porphyrin; urinary porphyrins in disease, 1298

Vaccination, Encephalitis Following: See under Encephalitis
Vander Veer, A.: Experiences with insulin shock therapy in schizophrenia, 907
Vasomotor System: See also Arteries
local neurogenous metabolic effects in vasoconstriction of central origin, 1076
vasomotor responses in hemiplegic patients, 1299
Veins: See also Embolism; Thrombosis; Vasomotor System; etc.
effect of carotid sinus on venous flow, 1301
Pressure in: See Blood pressure
vascular architecture of lesions of multiple sclerosis, *1
Ventriculography: See Brain, roentgenography
Vertebrae: See Spine
Vestibular Apparatus: See Ear, internal; Equilibrium
Nuclei: See Medulla Oblongata
Vibration, sensation of vibration with reference to its clinical significance, 1330

Viets, H. R.: Prostigmin in diagnosis and treatment of myasthenia gravis, 1349
Viruses, epidemic in mouse colony due to virus of acute lymphocytic choriomeningitis, 633
virus etiology of 1 form of lymphocytic meningitis, 866
Viscera, tumor syndrome with hyperthermia and visceral disorders due to chronic basilar tuberculous meningo-encephalitis, 166
Vision: See also Blindness
defects in visual field of 1 eye only in patients with lesion of 1 optic radiation, 652
effects of occipital lobectomy on vision in chimpanzee, 415
physiology; cerebral representation of retina in chimpanzee, 416
physiology; temporal and spatial summation of extrinsic impulses with intrinsic activity of cortex, 618
Vitamins, B_1 deficiency in rat's brain, 397
B, etiology of polyneuritis in alcohol addict, 875
C, studies in histochemistry; quantitative distribution of vitamin C in adrenal gland at various stages of development, 848
provitamin D of heat-treated cholesterol, 396
von Storch, T. J. C.: Factors producing lumbar cerebrospinal fluid pressure in man in erect posture, *1158
Voris, H. C.: Gunshot wound of head; report of case, 906

Waggoner, R. W.: Clinicopathologic study of astrocytomas, *1208
Ward, J. W.: Electrical stimulation of cortex cerebri of cats; responses elicitable in chronic experiments through implanted electrodes, *927
Water metabolism in relation to convulsions, *798
Watts, J. W.: Subcortical prefrontal lobotomy in treatment of certain psychoses, 225
Wechsler, I. S.: Dyskinesia; presentation of cases, 895
Excision of speech area without resultant aphasia, 430
Weil's Disease: See Jaundice, spirochetal
White, B. V., Jr.: "Cold pressor test" in tension and anxiety; cardiochronographic study, *964
White, P.: Mood—content problem and thymonoic reactions, *90
White, William Alanson, 608
Whitehorn, J. C.: Unsteadiness of heart rate in psychotic and neurotic states, *62
Whiting, I.: Environmental stress as precipitating factor for rheumatoid arthritis, 1348
Wigton, R.: Fracture dislocation in region of atlas and axis with consideration of delayed neurologic manifestations and roentgenographic features, 426
Wilson, Samuel Alexander Kinnier, 388
Winkelman, N. W.: Syphilis of spinal cord, 425
Wittels, F.: Transference phenomenon in case of phobia, 1116
Wolff, H. G.: Studies in diseases of muscle; metabolism of creatine and creatinine in progressive muscular dystrophy, *992
Word Blindness: See Aphasia, visual
Wortis, J.: Hypoglycemic treatment of psychoses; experiences at Bellevue Hospital, 191
Wound, gunshot, of head; report of case, 906

Yaskin, J. C.: Abscess of brain of undetermined etiology; report of 4 cases in which recovery occurred, 1124
Treatment of myasthenia gravis; report of 6 cases, 423
Yohimbine, action on autonomic nervous system, 1303
Young, B. R.: Air myelography in diagnosis of lesions of spinal canal with reference to those of nucleus pulposus and to "sciatic syndrome," 1126

Zeitlin, H.: Cystic tumor of third ventricle containing colloid material, *268
Zona: See Herpes zoster